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OM nucleic - nucleic search, using sw model

Run on: March 3, 2004, 09:32:18 ; Search time 639 Seconds
(without alignments)
10191.686 Million cell updates/sec

Title: US-10-074-547-3
Perfect score: 1533
Sequence: 1 atgtatacagtcagtaaga.....tggatgggcacatgttttag 1533

Scoring table: IDENTITY NUC

Gapop 10.0 , Gapext 1.0

Searched: 3373863 seqs, 212409041 residues

Total number of hits satisfying chosen parameters: 6747726

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : N_Geneseq_29Jan04:*

- 1: Geneseqn1980s:*
- 2: Geneseqn1990s:*
- 3: Geneseqn2000s:*
- 4: Geneseqn2001as:*
- 5: Geneseqn2001bs:*
- 6: Geneseqn2002s:*
- 7: Geneseqn2003as:*
- 8: Geneseqn2003bs:*
- 9: Geneseqn2003cs:*
- 10: Geneseqn2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	1533	100.0	4037	5	ABV26931
2	1533	100.0	4037	5	ABV21089
3	1533	100.0	4419	6	ABV53449
4	1529.8	99.8	3639	7	ABX71097
5	1521	99.2	2139	6	ABQ72638
6	1384.4	90.3	1867	7	AD36317
7	1062.4	69.3	3645	7	AD36317
8	671.8	43.8	1294	6	ABX97074
9	537.4	35.1	614	5	ABV22054
10	537.4	35.1	614	5	ABV40993
11	442	28.8	2838	7	AD36317
12	300.4	19.6	314	5	ABV10902
13	299.4	19.5	313	5	ABV01733
14	284.4	18.6	501	4	AAI87063
15	263.2	17.2	2681	7	AB235957
16	235	15.3	431	4	AAI89484
17	182.4	11.9	1568	6	ABN85745
18	182.4	11.9	2628	7	ABX70801
19	182.4	11.9	3440	6	ABK83222
20	180.8	11.8	3815	7	ABX56295
21	160.4	10.5	3321	6	ABX22365
22	158.4	10.3	387	6	ABN76577
23	147	9.6	2322	4	ABL06203

24	139	9.1	2531	7	ABZ25095
25	130.6	8.5	3238	4	ABL06109
26	130.6	8.5	6274	4	ABL06108
27	129.6	8.5	1982	4	AAS56593
28	129.6	8.5	1982	6	ABT11027
29	129.6	8.5	1982	7	ACC72760
30	129.6	8.5	1982	7	ACC72765
31	129.6	8.5	1982	7	ACC49538
32	129.6	8.5	2026	2	AAZ11734
33	127.4	8.3	602	2	AAV90044
34	127	8.3	1458	7	AAV55550
35	127	8.3	1548	7	AAV55565
36	127	8.3	1752	7	AAV55564
37	127	8.3	2241	6	AAV36309
38	127	8.3	2559	6	AAV35980
39	115.2	7.5	1458	7	AAV55577
40	115.2	7.5	1466	7	AAV55580
41	114.8	7.5	1344	6	ABL57731
42	114.8	7.5	1803	4	AAK94689
43	114.6	7.5	1278	6	AB53751
44	114.6	7.5	1281	6	ABQ86184
45	114.6	7.5	1375	6	ABL57732

ALIGNMENTS

RESULT 1
ABV26931
ID ABV26931 standard; cDNA; 4037 BP.
AC (ABV26931)
XX
DT 16-SEP-2002 (first entry)
XX
DE Human prostate-expression marker cDNA 26922.
XX
KW Human; prostate cancer; cytostatic; carcinogen; pharmacodynamic marker;
KW pharmacogenomic marker; gene; ss.
XX
OS Homo sapiens.
XX
FN WO200160860-A2.
XX
PD 23-AUG-2001.
XX
PF 20-FEB-2001; 2001WO-US005171.
XX
PR 17-FEB-2000; 2000US-0183319P.
PR 16-MAR-2000; 2000US-0189862P.
PR 25-MAY-2000; 2000US-0207454P.
PR 09-JUN-2000; 2000US-0211314P.
PR 18-JUL-2000; 2000US-0219007P.
PR 13-DEC-2000; 2000US-0255281P.
PA (MILL-) MILLENNIUM-PREDICTIVE-MEDICINE INC.
PI Schlegel R.; Endege WO.; Monahan JE;
XX WPI; 2001-662795/76.

Novel isolated nucleic acid molecule associated with cancerous state of prostate cells and correlating with presence of prostate cancer, useful for detecting presence of prostate cancer, stage of prostate cancer.

Claim 1; Page 5452-5453; 11750pp; English.

The invention relates to an isolated nucleic acid molecule (I) comprising a nucleotide sequence given in Tables 1-9 (ABV00010-ABV62213) of the specification or its complement. (I) is useful for: (a) assessing whether a patient is afflicted with prostate cancer; (b) monitoring the progression of prostate cancer in a patient; (c) assessing the efficacy of a test compound to inhibit prostate cancer in a patient; (d) assessing

Db 791 GCCTACCTGCGAGCGGCGGTCATGGTGGGAGGATTTCCAGAGAGAGCGCGCCCTCGCC 850
 Qy 481 CAGGGCTCAGCACACCGGAGCGGATTCGTTACGTTCTCTATGACTGCTGCTGGAAG 540
 Db 851 CAGGGCTCAGCACACCGGAGCGGATTCGTTACGTTCTCTATGACTGCTGCTGGAAG 910
 Qy 541 TACCTGTCGAGAGTACGCTGAGAGATGCGATGTTGATCAAGTGCCTTCCCTA 600
 Db 911 TACCTGTCGAGAGTACGCTGAGAGATGCGATGTTGATCAAGTGCCTTCCCTA 970
 Qy 601 AACCTGTCGTTGTCGGGCGCTCATGAGGCGCTCTCTCTGTTAAACCAACCAACGAC 660
 Db 971 AACCTGTCGTTGTCGGGCGCTCATGAGGCGCTCTCTCTGTTAAACCAACCAACGAC 1030
 Qy 661 CCAGAGAGAGATGTCGTCGCTGCGAGCGCATCCACAGATCTGTAAGTCAACT 720
 Db 1031 CCAGAGAGAGATGTCGTCGCTGCGAGCGCATCCACAGATCTGTAAGTCAACT 1090
 Qy 721 GGACAGAGAGAGATGTCGTCGCTGCGAGCGCATCCACAGATCTGTAAGTCAACT 780
 Db 1091 GGACAGAGAGAGATGTCGTCGCTGCGAGCGCATCCACAGATCTGTAAGTCAACT 1150
 Qy 781 GACCTGACGCGAGAGTGCCTGCGATCAGGCGGCGACAGAGAGATGTCGCTG 840
 Db 1151 GACCTGACGCGAGAGTGCCTGCGATCAGGCGGCGACAGAGAGATGTCGCTG 1210
 Qy 841 CGGATTCGAGAGTGTGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 900
 Db 1211 CGGATTCGAGAGTGTGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 1270
 Qy 901 TATTCGGGCTGTTGTCGAGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 960
 Db 1271 TATTCGGGCTGTTGTCGAGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 1330
 Qy 961 TATTCGGGCTGTTGTCGAGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 1020
 Db 1331 TATTCGGGCTGTTGTCGAGAGTGTGTCATGAGAGTGTGAGTGTGAGTGTGAGTGTG 1390
 Qy 1021 GTCAATTTGATTAATCTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1080
 Db 1391 GTCAATTTGATTAATCTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1450
 Qy 1081 ATAGTTCACATCTTTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1140
 Db 1451 ATAGTTCACATCTTTGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 1510
 Qy 1141 GTTTGGAATGCTTCTGTTGGGCAACTTCACTGCTGCTGCTGCTGCTGCTGCTGCTG 1200
 Db 1511 GTTTGGAATGCTTCTGTTGGGCAACTTCACTGCTGCTGCTGCTGCTGCTGCTGCTG 1570
 Qy 1201 TTGATGACACAGTACGCTGCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1260
 Db 1571 TTGATGACACAGTACGCTGCGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1630
 Qy 1261 TATTTCTCCCTAATGCGCGTAGTGAAGTGTGTTGGGAGAGAGAGAGAGAGAGAGAG 1320
 Db 1631 TATTTCTCCCTAATGCGCGTAGTGAAGTGTGTTGGGAGAGAGAGAGAGAGAGAGAG 1690
 Qy 1321 GCCTACGGCATCATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1380
 Db 1691 GCCTACGGCATCATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1750
 Qy 1381 GGGTGGATCATGACATCAGCAAAATATGATTTTCTCTTACATATGCTGCTGCTGCTGCT 1440
 Db 1751 GGGTGGATCATGACATCAGCAAAATATGATTTTCTCTTACATATGCTGCTGCTGCTGCT 1810
 Qy 1441 TACATGATGATGATCTCTTTTACTTATTCAGCGCTGCTGCTGCTGCTGCTGCTGCTGCT 1500
 Db 1811 TACATGATGATGATCTCTTTTACTTATTCAGCGCTGCTGCTGCTGCTGCTGCTGCTGCT 1870
 Qy 1501 AGAGAGAGAGATGATGATGATGATGATGATGATGATGATGATGATGATGATGATGAT 1533

Db 1871 AGAGAGAGAGATGATGATGATGATGATGATGATGATGATGATGATGATGATGATGAT 1903

RESULT 4
 US-10-380-727-46
 ; Sequence 46 Application US/10380727
 ; Publication No. US20040024183A1
 ; GENERAL INFORMATION:
 ; INCYTE GENOMICS, INC.; LEE, Ernestine A.;
 ; APPLICANT: CHUE, Henry; LAL, Preeti G.;
 ; APPLICANT: CHAMLA, Narinder K.; BAUGHN, Mariah R.;
 ; APPLICANT: WARRAN, Bridget A.; LEE, Sally;
 ; APPLICANT: SANJANWALA, Madhu S.; YAO, Monique G.;
 ; APPLICANT: RAMKUMAR, Jayalaxmi; THORNTON, Michael;
 ; APPLICANT: GANDHI, Amena R.; POLICKY, Jennifer L.;
 ; APPLICANT: ELLIOTT, Vicki S.; ARVIZU, Chandra;
 ; APPLICANT: RAUMANN, Brigitte E.; BRUNS, Christopher M.;
 ; APPLICANT: RAUNA, Amir; HAFALIA, April J.A.;
 ; APPLICANT: NGUYEN, Damiel B.; XU, Yuming;
 ; APPLICANT: LU, Dying Aina M.; ISON, Craig H.;
 ; APPLICANT: GRIFFIN, Jennifer A.; REDDY, Roopa M.;
 ; APPLICANT: BURFORD, Neil
 ; TITLE OF INVENTION: TRANSPORTERS AND ION CHANNELS
 ; FILE REFERENCE: PI-0217 USN
 ; CURRENT APPLICATION NUMBER: US/10380,727
 ; CURRENT FILING DATE: 2003-03-14
 ; PRIOR APPLICATION NUMBER: PCT/US01/28938
 ; PRIOR FILING DATE: 2001-09-14
 ; PRIOR APPLICATION NUMBER: US 60/241,700
 ; PRIOR FILING DATE: 2000-10-18
 ; PRIOR APPLICATION NUMBER: US 60/240,540
 ; PRIOR FILING DATE: 2000-10-13
 ; PRIOR APPLICATION NUMBER: US 60/239,057
 ; PRIOR FILING DATE: 2000-10-05
 ; PRIOR APPLICATION NUMBER: US 60/236,882
 ; PRIOR FILING DATE: 2000-09-29
 ; PRIOR APPLICATION NUMBER: US 60/234,842
 ; PRIOR FILING DATE: 2000-09-22
 ; PRIOR APPLICATION NUMBER: US 60/232,685
 ; PRIOR FILING DATE: 2000-09-15
 ; NUMBER OF SEQ ID NOS: 52
 ; SOFTWARE: PERL Program
 ; SEQ ID NO 46
 ; LENGTH: 1867
 ; TYPE: DNA
 ; ORGANISM: Homo sapiens
 ; FEATURE:
 ; NAME/KEY: misc feature
 ; OTHER INFORMATION: Incyte ID No. US20040024183A1 3586648CB1
 ; US-10-380-727-46

Query Match 90.3%; Score 1384.4; DB 16; Length 1867;
 Best Local Similarity 99.6%; Pred. No. 0;
 Matches 1388; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

Qy 1 ATGTATACAGTCATGAAGATATTTGGTATGATTTTGAAGATGCGCCCAAGACAAAAG 60
 Db 386 ATGTATACAGTCATGAAGATATTTGGTATGATTTTGAAGATGCGCCCAAGACAAAAG 445
 Qy 61 ACACGTGAGCCGCCCAACCAATTTGATGCGGATGGGCTTGGATGATGGTCTCTCTCT 120
 Db 446 ACACGTGAGCCGCCCAACCAATTTGATGCGGATGGGCTTGGATGATGGTCTCTCTCT 505
 Qy 121 TTCTTTTGTGCACATCTCTCATCATGCGCTCCAGATGCGCCCTGGGTGCTCTCAACGTGAA 180
 Db 506 TTCTTTTGTGCACATCTCTCATCATGCGCTCCAGATGCGCCCTGGGTGCTCTCAACGTGAA 565
 Qy 181 TGGCTGGAGATTTCCACAGAGCCGCGCTGACCGGCTGGGTGCTGCTGCTGCTGCTGCTG 240
 Db 566 TGGCTGGAGATTTCCACAGAGCCGCGCTGACCGGCTGGGTGCTGCTGCTGCTGCTGCTG 625
 Qy 241 GGCATCACCTTTCATGATGGGCTTTCATCGGCTTTCATTAACACCTGTTGGGTGCGGC 300

Db 626 GGCAATCACCTTGATAGTGGGCCCTTTTCATCGGCTTGTTCATTAAACACCTGTGGTGCCGC 685
 Qy 301 CAGACTGGCATCACTGGAGGCTCGTCAACTCCCTGGGCTGGTGTGAGTGCCTATGCT 360
 Db 686 CAGACTGGCATCACTGGAGGCTCGTCAACTCCCTGGGCTGGTGTGAGTGCCTATGCT 745
 Qy 361 GCAAAAGTGCATTATCTCTTTCATTACTTTTGGAGTCGCAGCTGGCTGGGCGAGCGGATG 420
 Db 746 GCAAAAGTGCATTATCTCTTTCATTACTTTTGGAGTCGCAGCTGGCTGGGCGAGCGGATG 805
 Qy 421 GCTACTGTCGACGGTGTGTCATGTTGGGAGGTATTTCCAGAGAGACGCGCCCTCGCC 480
 Db 806 GCTACTGTCGACGGTGTGTCATGTTGGGAGGTATTTCCAGAGAGACGCGCCCTCGCC 865
 Qy 481 CAGGGCTCAGCACACGCGGACCGGATTCGGTACGTTCTCTAATGACTGTGTGCTGAG 540
 Db 866 CAGGGCTCAGCACACGCGGACCGGATTCGGTACGTTCTCTAATGACTGTGTGCTGAG 925
 Qy 541 TACCTGTGGCGAGTACGGCTGGAGGAATGCCATGTTGATCCAAAGTCCCGTTCCCTA 600
 Db 926 TACCTGTGGCGAGTACGGCTGGAGGAATGCCATGTTGATCCAAAGTCCCGTTCCCTA 985
 Qy 601 AACCTGTGTTTGTGGGCGCTCATGAGGCGCTCTCTCTGTTGTAATAAACCCAAACGAC 660
 Db 986 AACCTGTGTTTGTGGGCGCTCATGAGGCGCTCTCTCTGTTGTAATAAACCCAAACGAC 1045
 Qy 661 CCAGGAGAGAAAGTGTGGTGGCTCCAGCGCACTCCACAGAACTGTGGAAGTCACT 720
 Db 1046 CCAGGAGAGAAAGTGTGGTGGCTCCAGCGCACTCCACAGAACTGTGGAAGTCACT 1105
 Qy 721 GGACAGCAGGGAAGAAACAGAGAGAGAGTGTGGCTCGGGAACGAGGAGACCTCTGC 780
 Db 1106 GGACAGCAGGGAAGAAACAGAGAGAGAGTGTGGCTCGGGAACGAGGAGACCTCTGC 1165
 Qy 781 GACCTGACGCCAGAGTGGCCCGATCAGGCGGSCACAGAGAAACATGTGCGCCTC 840
 Db 1166 GACCTGACGCCAGAGTGGCCCGATCAGGCGGSCACAGAGAAACATGTGCGCCTC 1225
 Qy 841 CGGATTCGAAGACTCTCAGCTGGCTCACCATGAGTCAAGAGGCTTCAGGAGTGG 900
 Db 1226 CGGATTCGAAGACTCTCAGCTGGCTCACCATGAGTCAAGAGGCTTCAGGAGTGG 1285
 Qy 901 TATTCGGGCTACTTTGGGACAGCTCTCTATTTCATATGAAATGTTGTAGCCTTTAT 960
 Db 1286 TATTCGGGCTACTTTGGGACAGCTCTCTATTTCATATGAAATGTTGTAGCCTTTAT 1345
 Qy 961 TTCTGGGCTTTGTTGATACAGCTTTGTCATCCCTTTTCATTCACCTCCAGAAATC 1020
 Db 1346 TTCTGGGCTTTGTTGATACAGCTTTGTCATCCCTTTTCATTCACCTCCAGAAATC 1405
 Qy 1021 GTCAATTTGTATACTTATCGGAGCAAAACGACGTTTTCCTCTGACGTCATATATAGCA 1080
 Db 1406 GTCAATTTGTATACTTATCGGAGCAAAACGACGTTTTCCTCTGACGTCATATATAGCA 1465
 Qy 1081 ATAGTTGACATCTTTGGAAGATGATCTGGGCTCATAGCGGACTTTCGCTTGCATAGT 1140
 Db 1466 ATAGTTGACATCTTTGGAAGATGATCTGGGCTCATAGCGGACTTTCGCTTGCATAGT 1525
 Qy 1141 GTTTGGAATGCTCTCTGTTGGCAACTTCACCTTTGCTCCTCAGTATTTTATCTGCG 1200
 Db 1526 GTTTGGAATGCTCTCTGTTGGCAACTTCACCTTTGCTCCTCAGTATTTTATCTGCG 1585
 Qy 1201 TTGATGACACGTCAGCTGGCTGGCGCTCATCTGTGCGCTGATAGGGTTTTCAGTGGT 1260
 Db 1586 TTGATGACACGTCAGCTGGCTGGCGCTCATCTGTGCGCTGATAGGGTTTTCAGTGGT 1645
 Qy 1261 TATTTCTCCCTAATGCCGTFAGTGAAGTGTGGGCTTGGTTCGATTCGACACCTTGGCCAT 1320
 Db 1646 TATTTCTCCCTAATGCCGTFAGTGAAGTGTGGGCTTGGTTCGATTCGACACCTTGGCCAT 1705
 Qy 1321 GCCTAGGCAATCATCATCTGTGCTAATGGAATCTCTGCACTCTGCACTTCTGCACTTTTGA 1380
 Db 1706 GCCTAGGCAATCATCATCTGTGCTAATGGAATCTCTGCACTTCTGCACTTTTGA 1765

RESULT 5
 US-10-094-749-357
 ; Sequence 357, Application US/10094749
 ; Publication No. US20030219741A1
 ; GENERAL INFORMATION:
 ; APPLICANT: ISOGAI, TAKAO
 ; APPLICANT: SUGIYAMA, TOMOYASU
 ; APPLICANT: OTSUKI, TETSUJI
 ; APPLICANT: WAKAMATSU, AI
 ; APPLICANT: SATO, HIROYUKI
 ; APPLICANT: ISHII, SHIZUKO
 ; APPLICANT: YAMAMOTO, JUN-ICHI
 ; APPLICANT: ISONO, YUUKO
 ; APPLICANT: HIO, YURI
 ; APPLICANT: OTSUKA, KAORU
 ; APPLICANT: NAGAI, KEIICHI
 ; APPLICANT: IRIE, RYOTARO
 ; APPLICANT: TAMECHIKA, ICHIRO
 ; APPLICANT: SEKI, NAOHICO
 ; APPLICANT: YOSHIKAWA, TSUTOMU
 ; APPLICANT: OTSUKA, MOTOYUKI
 ; APPLICANT: NAGAHARI, KENJI
 ; APPLICANT: MASUHO, YASUHIKO
 ; TITLE OF INVENTION: NOVEL FULL-LENGTH cDNA
 ; FILE REFERENCE: 084335/0160
 ; CURRENT APPLICATION NUMBER: US/10/094,749
 ; PRIOR FILING DATE: 2002-03-12
 ; PRIOR APPLICATION NUMBER: 60/350,435
 ; PRIOR FILING DATE: 2002-01-24
 ; PRIOR APPLICATION NUMBER: JP 2001-328381
 ; PRIOR FILING DATE: 2001-09-14
 ; NUMBER OF SEQ ID NOS: 3381
 ; SOFTWARE: PatentIn Ver. 2.1
 ; SEQ ID NO 357
 ; LENGTH: 3645
 ; TYPE: DNA
 ; ORGANISM: Homo sapiens
 US-10-094-749-357

Query Match 69.3%; Score 1062.4; DB 15; Length 3645;
 Best Local Similarity 99.9%; Pred. No. 0;
 Matches 1063; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
 Qy 470 GCGCCCTCGCCAGGGGCTCAGCACCGGGACCGGATTCGGTACGTTCTCTAATGACTG 529
 Db 186 GCGCCCTCGCCAGGGGCTCAGCACCGGGACCGGATTCGGTACGTTCTCTAATGACTG 245
 Qy 530 TGCTGCTGAAGTACCTGTGGCGAGATACGGCTGAGAGGAATGCCATGTTGATCCAGGTTG 589
 Db 246 TGCTGCTGAAGTACCTGTGGCGAGATACGGCTGAGAGGAATGCCATGTTGATCCAGGTTG 305
 Qy 590 CCGTTTCCCTAAACCTGTGTTTGGGGCGCTCATAGAGGCCCTCTCTCCTGTGTAATA 649
 Db 306 CCGTTTCCCTAAACCTGTGTTTGGGGCGCTCATAGAGGCCCTCTCTCCTGTGTAATA 365
 Qy 650 ACCCAAAACGACCCAGGAGAGAAAGATGTGCTGGCTCGCCAGCGCACTCCACAGAAATCTG 709
 Db 366 ACCCAAAACGACCCAGGAGAGAAAGATGTGCTGGCTCGCCAGCGCACTCCACAGAAATCTG 425
 Qy 710 TGAAGTCAACTGACACGAGGAGAGAAACAGAGAGAGGATGGTGGGCTCGGGAAACGAGG 769
 Db 426 TGAAGTCAACTGACACGAGGAGAGAAACAGAGAGAGGATGGTGGGCTCGGGAAACGAGG 485
 Qy 770 AGACCCCTCTGCGACCTGCAAGCCAGAGTCCCGGATCAGCGCGGACACAGAAAGAAACA 829
 Db 486 AGACCCCTCTGCGACCTGCAAGCCAGAGTCCCGGATCAGCGCGGACACAGAAAGAAACA 545

DB:	13	Gaps:	0
US-10-074-547-2	(1-510) x US-10-074-547-1	(1-4419)	
QY	1	MetTyrThrSerHisGluAspIleGlyTyrAspPheGluAspGlyProLysAspLysLys	20
Db	449	ATGTAATACCAGTCATGAAGATATTTGGTATGATTTTGAAGATGCGCCCAAGACAAAAG	508
QY	21	ThrLeuLysProHisProAsnIleAspGlyGlyTyrAlaTyrMetMetValLeuSerSer	40
Db	509	ACACTGAAGCCCAACCCAAACATTTGATGGCGGATGGCTTGGAGTGAATGGTCTCTCTCT	568
QY	41	PhePheValHisIleLeuIleMetGlySerGlnMetAlaLeuGlyValLeuAsnValGlu	60
Db	569	TTCTTTGTGCACATCTTCATCATGGGCTCCAGATGGCTCTGGTGTCTCTCAACGTGAAA	628
QY	61	TyrLeuGluGluPheHisGlnSerArgGlyLeuThrAlaTyrValSerSerLeuSerMet	80
Db	629	TGGCTGGAGAAATTCACACAGAGCGCGGCTGCACCGCTGGGTCACTCCCTCAGCATG	688
QY	81	GlyIleThrLeuIleValGlyProPheIleGlyLeuPheIleAsnThrCysGlyCysArg	100
Db	689	GGCATCACCTTGATAGTGGGCCCTTTTCATCGGCTTGTTCAATTAACACTGTGGGTGCCG	748
QY	101	GlnThrAlaIleIleGlyGlyLeuValAsnSerLeuGlyTyrValLeuSerAlaTyrAla	120
Db	749	CAGACTCGCATCATGGAGGGCTCGTCAACTCCCTGGGCTGGTGTGTAGTGCTATGCT	808
QY	121	AlaAsnValHisTyrLeuPheIleThrPheGlyValAlaIleGlyLeuGlySerGlyMet	140
Db	809	GCAAAAGTGCATATATCTCTTCATTACTATTTGGAGTGCAGCTGGCTGGGACGCGGATG	868
QY	141	AlaTyrLeuProAlaValValMetValGlyArgTyrPheGlnLysArgArgAlaLeuAla	160
Db	869	GCCTACTGCGACGGGTGGTCACTGGTGGGACAGTATTTCCAGAAGACACGCGCCTCGCC	928
QY	161	GlnGlyLeuSerThrThrGlyThrGlyPheGlyThrPheLeuMetThrValLeuLeuLys	180
Db	929	CAGGGCTCAGCACCAACGGGACCGGATTCGGTACGTTCCTTAATGACTGTGCTGCTGAAG	988
QY	181	TyrLeuCysAlaGluTyrGlyTyrArgAsnAlaMetLeuIleGlnGlyAlaValSerLeu	200
Db	989	TACTGTGGCGAGTAGTACGCTGGAGGAATGCCATGTGTATCCAGAGTGCGTGTCCCTA	1048
QY	201	AsnLeuCysValCysGlyAlaLeuMetArgProLeuSerProGlyLysAsnProAsnAsp	220
Db	1049	AACCTGTGTGTTGTGGGGCGCTCATCAGGGCCCTCTCTCTGTGTAACCAACCAACACAC	1108
QY	221	ProGlyGluLysAspValArgGlyLeuProAlaHisSerThrGluSerValLysSerThr	240
Db	1109	CCAGGACAGAAAGATGTGCGTGGCTCTCCACGGCACCTCCACAGAAATCTGTGAAGTCAACT	1168
QY	241	GlyGlnGlnGlyArgThrGluGluLysAspGlyGlyLeuGlyAsnGluThrLeuCys	260
Db	1169	GGACAGCAGGGAAGAAACAGAGAGAGATGTTGGGCTCGGGAACGAGGAGACCTCTGCG	1228
QY	261	AspLeuGlnAlaGlnGluCysProAspGlnAlaGlyHisArgLysAsnMetCysAlaLeu	280
Db	1229	GACCTGCAAGCCCAAGAGTGTCCCGCATCAGGCGGGCACAGAGAAGAAACATGTGTGGCCCTC	1288
QY	281	ArgIleLeuLysThrValSerTyrLeuThrMetArgValArgLysGlyPheGluAspTyr	300
Db	1289	CGGATTTGAAAGATCTGTCAAGCTGGCTCACCATGAGATCAGGAAGGGCTTCAGAGACTGG	1348
QY	301	TyrSerGlyTyrPheGlyThrAlaSerLeuPheThrAsnArgMetPheValAlaPheIle	320
Db	1349	TATTTCGGGCTACTTTTGGACAGCCCTCTCTATTTTACAAATCCAAATGTTTGTAGCCCTTATT	1408
QY	321	PheTyrAlaLeuPheAlaTyrSerSerPheValIleProPheIleHisLeuProGluIle	340
Db	1409	TTCTGGGGCTTTGTTTGCATACAGACAGCTTGTGTATCCCTCTCATTCACCTCCCAAGAAATC	1468
QY	341	ValAsnLeuTyrAsnLeuSerGluGlnAsnAspValPheProLeuThrSerIleAla	360

QY 1 MetTyrThrSerHisGluAspIleGlyTyrAspPheGluAspGlyProValSerAspValys 20
DB 371 ATGATATACCATCATGAGATATTTGGGTATGATTTTGAAGATGGCCCCCAAGACAAAG 430
QY 21 ThrLeuLysProHisProAsnIleAspGlyGlyTyrPalaTrpMetMetValLeuSerSer 40
DB 431 ACACTGAAGCCCCCAACAAACATTGATGAGGGGATGGGCTTGGATGATGCTCTCTCT 490
QY 41 PhePheValHisIleLeuIleMetGlySerGlnMetAlaLeuGlyValLeuAsnValGlu 60
DB 491 TTCCTTGGACATCTCATCATGCGGTCCAGATGGCCCTGGGTGCTCTCAACGTGGNA 550
QY 61 TrpLeuGluGluPheHisGlnSerArgGlyLeuThrAlaTrpValSerSerLeuSerMet 80
DB 551 TGGCTGGAGAAATTCACACAGAGCCGGGCTGACCGCTGGGCTCAGCTCCCTCAGCATG 610
QY 81 GlyIleThrIleValGlyProPheIleGlyLeuPheIleAsnThrCysGlyCysArg 100
DB 611 GGCATCACCTGATAGTGGGCTCTTTCATCGGCTGTTCATTAACACCTGTGGGTGGCC 670
QY 101 GlnThrAlaIleIleGlyLeuValAsnSerLeuGlyTyrValLeuSerAlaTyrAla 120
DB 671 CAGACTGGATCATTTGAGGGCTCGTCAACTCCCTGGGCTGGGTGTGAGTGGCTATGCT 730
QY 121 AlaAsnValHisTyrLeuPheIleThrPheGlyValAlaAlaGlyLeuGlySerGlyMet 140
DB 731 GCACACGTGCTATTCCTTCATTTTGGAGTGGCAGCTGGCTGGGCTGGGAGGGGATG 790
QY 141 AlaTyrLeuProAlaValMetValGlyArgTyrPheGlnLysArgAlaLeuAla 160
DB 791 GCCTACCTGCCAGCGGTGCTCATGCTGGGAGTGGCAGCTGGCTGGGCTGGGAGGGGATG 850
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QY 261 AspLeuGlnAlaGlnGluCysProAspGlnAlaGlyHisArgLysAsnMetCysAlaLeu 280
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DB 1211 CGGATTCGAGAGCTGTGAGTGGCTCACCATGAGACTCAGAGAGGCTTCGAGGACTGG 1270
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501 ArgArgLysTyrMetAspGlyAlaHisVal 510
1871 AGAAGAAATACATGATGGTGCACATGTT 1900

RESULT 4
US-10-380-727-46
; Sequence 46, Application US/10380727
; Publication No. US20040024183A1
; GENERAL INFORMATION:
; APPLICANT: INCYTE GENOMICS, INC.; LEE, Ernestine A.;
; APPLICANT: YUE, Henry; LAL, Preeti G.;
; APPLICANT: CHAWLA, Narinder K.; BAUGHN, Mariah R.;
; APPLICANT: WARREN, Bridget A.; LEE, Sally;
; APPLICANT: SANJANWALA, Madhu S.; YAO, Monique G.;
; APPLICANT: RAMKUMAR, Jayalaxmi; THORNTON, Michael;
; APPLICANT: GANDHI, Ameena R.; POLICKY, Jennifer L.;
; APPLICANT: ELLIOTT, Vicki S.; ARVIZU, Chandra;
; APPLICANT: RAUMANN, Brigitte E.; BRUNS, Christopher M.;
; APPLICANT: NAINA, Amir; HAFALIA, April J.A.;
; APPLICANT: NGUYEN, Dannel B.; XU, Yuming;
; APPLICANT: LU, Dyung Aina M.; ISON, Craig H.;
; APPLICANT: GRIFFIN, Jennifer A.; REDDY, Roopa M.;
; APPLICANT: BURFORD, Neil
; TITLE OF INVENTION: TRANSPORTERS AND ION CHANNELS
; FILE REFERENCE: PI-0217 USN
; CURRENT APPLICATION NUMBER: US/10/380,727
; CURRENT FILING DATE: 2003-03-14
; PRIOR APPLICATION NUMBER: PCT/US01/28938
; PRIOR FILING DATE: 2001-09-14
; PRIOR APPLICATION NUMBER: US 60/241,700
; PRIOR FILING DATE: 2000-10-18
; PRIOR APPLICATION NUMBER: US 60/240,540
; PRIOR FILING DATE: 2000-10-13
; PRIOR APPLICATION NUMBER: US 60/239,057
; PRIOR FILING DATE: 2000-10-05
; PRIOR APPLICATION NUMBER: US 60/236,882
; PRIOR FILING DATE: 2000-09-29
; PRIOR APPLICATION NUMBER: US 60/234,842
; PRIOR FILING DATE: 2000-09-22
; PRIOR APPLICATION NUMBER: US 60/232,685
; PRIOR FILING DATE: 2000-09-15
; NUMBER OF SEQ ID NOS: 52
; SOFTWARE: PERL Program
; SEQ ID NO 46
; LENGTH: 1867

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 Qy 461 GlyTyrIleTyrAspIle 466
 Db 1597 GGTAAACTCTCTGAGGTT 1614

RESULT 5
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 DEFINITION Sequence 46 from Patent WO0222684
 ACCESSION AX405579
 VERSION AX405579.1 GI:21438604
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 SOURCE Homo sapiens (human)

ORGANISM
 Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE
 AUTHORS Lee, B.-A., Yue, H., Lal, P. G., Wallia, N. K., Baughn, M. R., Warren, B.-A.,
 Gandhi, A. R., Pollick, J. L., Elliott, V. S., Arvizu, C., Raumann, B. E.,
 Bruns, C. M., Naini, A., Hafalia, A. J., Nguyen, D. B., Xu, Y., Lu, D. A.,
 Ison, C. H., Griffin, J. A., Reddy, R. M. and Burford, N.
 TITLE Transporters and ion channels
 JOURNAL Patent: WO 0222684-A 46 21-MAR-2002;
 Incyte Genomics, Inc. (US)

FEATURES
 source
 1. 1867
 Location/Qualifiers
 /organism="Homo sapiens"
 /mol_type="unassigned DNA"
 /db_xref="taxon:9606"
 /note="Incyte ID No: 3586648CB1"

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 Pred. No.: 1.65e-204 Length: 1867
 Score: 2433.00 Matches: 461
 Percent Similarity: 99.57% Conservative: 3
 Best Local Similarity: 98.93% Mismatches: 2
 Query Match: 90.24% Indels: 0
 DB: 6 Gaps: 0

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 Db 446 ACACCTGAAGCCCAACCAACCAATTTGATGGGATGGGCTTGGATGGTGTCTCTCTCT 505
 41 PhePheValHisIleLeuIleMetGlySerGlnMetAlaLeuGlyValLeuAsnValGlu 60

Db 506 TTCTTTGTGCATCTCTCATCTGCGCTCCAGATGGCCCTGGGTGTCTCAACGTGGAA 565
 Qy 61 TrpLeuGluGluPheHisGlnSerArgGlyLeuThrAlaTyrValSerSerLeuSerMet 80
 Db 566 TGGCTGGAGAAATTCACACAGAGCCGCGCTGACCGCTGGGTCACTCTCTCAGCATG 625
 Qy 81 GlyIleThrLeuIleValGlyProPheIleGlyLeuPheIleAsnThrCysGlyCysArg 100
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 Qy 101 GlnThrAlaIleIleGlyLeuValAsnSerLeuGlyTyrValLeuSerAlaTyrAla 120
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 Db 1526 GTTTGGAATCTCTCTCTTGTGGCCAACTTCACTCTGCTCTCTCTCTCTCTCTCTCTCTCT 1585
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 This clone was selected for full length sequencing because it
 passed the following selection criteria: Hexamer frequency ORF
 analysis.

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FILE 'SCISEARCH' ENTERED AT 14:07:00 ON 04 MAR 2004

COPYRIGHT 2004 THOMSON ISI

=> s monocarboxylate(w)transporter?

L1 997 MONOCARBOXYLATE(W) TRANSPORTER?

=> s slc16

L2 8 SLC16

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 5 DUP REM L2 (3 DUPLICATES REMOVED)

=> d ibib abs 1-5

L3 ANSWER 1 OF 5

MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 2004068746 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 12739169

TITLE: The SLC16 gene family-from monocarboxylate transporters (MCTs) to aromatic amino acid transporters and beyond.

AUTHOR: Halestrap Andrew P; Meredith David

CORPORATE SOURCE: Department of Biochemistry, University of Bristol, BS8 1TD, Bristol, UK, . A.Halestrap@Bristol.ac.uk

SOURCE: Pflugers Archiv : European journal of physiology, (2004 Feb) 447 (5) 619-28.

Journal code: 0154720. ISSN: 0031-6768.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20040211

Last Updated on STN: 20040211

AB The monocarboxylate cotransporter (MCT) family now comprises 14 members, of which only the first four (MCT1-MCT4) have been demonstrated experimentally to catalyse the proton-linked transport of metabolically

important monocarboxylates such as lactate, pyruvate and ketone bodies. SLC16A10 (T-type amino-acid transporter-1, TAT1) is an aromatic amino acid transporter whilst the other members await characterization. MCTs have 12 transmembrane domains (TMDs) with intracellular N- and C-termini and a large intracellular loop between TMDs 6 and 7. MCT1 and MCT4 require a monotopic ancillary protein, CD147, for expression of functional protein at the plasma membrane. Lactic acid transport across the plasma membrane is fundamental for the metabolism of and pH regulation of all cells, removing lactic acid produced by glycolysis and allowing uptake by those cells utilizing it for gluconeogenesis (liver and kidney) or as a respiratory fuel (heart and red muscle). The properties of the different MCT isoforms and their tissue distribution and regulation reflect these roles.

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:712649 CAPLUS
DOCUMENT NUMBER: 140:125986
TITLE: Diversity of amino acid transporters: molecular basis of disorder of amino acid metabolism
AUTHOR(S): Kanai, Yoshikatsu
CORPORATE SOURCE: School of Medicine and Pharmacology, Kyorin University, Japan
SOURCE: Molecular Medicine (Tokyo, Japan) (2003), 40(7), 782-790
CODEN: MOLMEL; ISSN: 0918-6557
PUBLISHER: Nakayama Shoten
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. The topics included are (1) diversity of amino acid transporters discussing the families of SLC1, SLC6, SLC7, **SLC16**, SLC25 and SLC38; (2) transepithelial amino acid transporters for neutral, basic and acidic amino acids in intestine and kidney; and (3) amino acid transporter abnormalities in cystinuria, lysinuric protein intolerance, Hartnup disorder, blue diaper syndrome, cystinosis and citrullinemia.

L3 ANSWER 3 OF 5 MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2003548466 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12946269
TITLE: The loop between helix 4 and helix 5 in the monocarboxylate transporter MCT1 is important for substrate selection and protein stability.
AUTHOR: Galic Sandra; Schneider Hans-Peter; Broer Angelika; Deitmer Joachim W; Broer Stefan
CORPORATE SOURCE: School of Biochemistry & Molecular Biology, Australian National University, Canberra ACT 0200, Australia.
SOURCE: Biochemical journal, (2003 Dec 1) 376 (Pt 2) 413-22.
Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031121
Last Updated on STN: 20031219
Entered Medline: 20031202

AB Transport of lactate, pyruvate and the ketone bodies acetoacetate and beta-hydroxybutyrate, is mediated in most mammalian cells by members of the monocarboxylate transporter family (**SLC16**). A conserved signature sequence has been identified in this family, which is located in the loop between helix 4 and helix 5 and extends into helix 5. We have mutated residues in this signature sequence in the rat monocarboxylate

transporter (MCT1) to elucidate the significance of this region for monocarboxylate transport. Mutation of R143 and G153 resulted in complete inactivation of the transporter. For the MCT1(G153V) mutant this was explained by a failure to reach the plasma membrane. The lack of transport activity of MCT1(R143Q) could be partially rescued by the conservative exchange R143H. The resulting mutant transporter displayed reduced stability, a decreased V (max) of lactate transport but not of acetate transport, and an increased stereoselectivity. Mutation of K137, K141 and K142 indicated that only K142 played a significant role in the transport mechanism. Mutation of K142 to glutamine resulted in an increase of the K (m) for lactate from 5 mM to 12 mM. In contrast with MCT1(R143H), MCT1(K142Q) was less stereoselective than the wild-type. A mechanism is proposed that includes all critical residues.

L3 ANSWER 4 OF 5 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2004:10980 SCISEARCH

THE GENUINE ARTICLE: 753UY

TITLE: The loop between helix 4 and helix 5 in the monocarboxylate transporter MCT1 is important for substrate selection and protein stability

AUTHOR: Galic S; Schneider H P; Broer A; Deitmer J W; Broer S (Reprint)

CORPORATE SOURCE: Australian Natl Univ, Sch Biochem & Mol Biol, Canberra, ACT 0200, Australia (Reprint); Univ Kaiserslautern, FB Biol, Abt Allgemeine Zool, D-67653 Kaiserslautern, Germany

COUNTRY OF AUTHOR: Australia; Germany

SOURCE: BIOCHEMICAL JOURNAL, (1 DEC 2003) Vol. 376, Part 2, pp. 413-422.

Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND.

ISSN: 0264-6021.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transport of lactate, pyruvate and the ketone bodies acetoacetate and beta-hydroxybutyrate, is mediated in most mammalian cells by members of the monocarboxylate transporter family (SLC16). A conserved signature sequence has been identified in this family, which is located in the loop between helix 4 and helix 5 and extends into helix 5. We have mutated residues in this signature sequence in the rat monocarboxylate transporter (MCT1) to elucidate the significance of this region for monocarboxylate transport. Mutation of R143 and G153 resulted in complete inactivation of the transporter. For the MCT1(G153V) mutant this was explained by a failure to reach the plasma membrane. The lack of transport activity of MCT1(R143Q) could be partially rescued by the conservative exchange R143H. The resulting mutant transporter displayed reduced stability, a decreased V-max of lactate transport but not of acetate transport, and an increased stereoselectivity. Mutation of K137, K141 and K142 indicated that only K142 played a significant role in the transport mechanism. Mutation of K142 to glutamine resulted in an increase of the Km for lactate from 5 mM to 12 mM. In contrast with MCT1(R143H), MCT1(K142Q) was less stereoselective than the wild-type. A mechanism is proposed that includes all critical residues.

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:634317 CAPLUS

DOCUMENT NUMBER: 137:180837

TITLE: cDNA and protein sequences of human monocarboxylate transporter sequence homolog protein 25466 and their uses

INVENTOR(S): Curtis, Rory A. J.
 PATENT ASSIGNEE(S): Millenium Pharmaceuticals, Inc., USA
 SOURCE: Eur. Pat. Appl., 57 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233024	A2	20020821	EP 2002-251056	20020215
EP 1233024	A3	20020918		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002132301	A1	20020919	US 2002-74547	20020212
PRIORITY APPLN. INFO.:			US 2001-269072P	P 20010215

AB The invention provides cDNA and protein sequences of human protein. The protein 25466 shares sequence homol. to monocarboxylate (MCT) transporters, and in particular to **SLC16** family members. The invention also provides antisense nucleic acid mols., recombinant expression vectors containing 25466 gene., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 25466 gene has been introduced or disrupted. The invention still further provides isolated 25466 proteins, fusion proteins, antigenic peptides and anti-25466 antibodies. Diagnostic and therapeutic methods utilizing compns. of the invention are also provided.

=> d his

(FILE 'HOME' ENTERED AT 14:04:47 ON 04 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:07:00 ON 04 MAR 2004

L1 997 S MONOCARBOXYLATE(W) TRANSPORTER?
 L2 8 S SLC16
 L3 5 DUP REM L2 (3 DUPLICATES REMOVED)

=> s l1(s) (family or superfamily)

L4 113 L1(S) (FAMILY OR SUPERFAMILY)

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 40 DUP REM L4 (73 DUPLICATES REMOVED)

=> s mct4 or mct?4

'?' TRUNCATION SYMBOL NOT VALID WITHIN 'MCT?4'

The truncation symbol ? may be used only at the end of a search term. To specify a variable character within a word use '!', e.g., 'wom!n' to search for both 'woman' and 'women'. Enter "HELP TRUNCATION" at an arrow prompt (=>) for more information.

=> s mct4 or mct!4

L6 214 MCT4 OR MCT!4

=> s l6 and l1

L7 190 L6 AND L1

=> dup rem l7

PROCESSING COMPLETED FOR L7

10/074547

04/03/2004

L8 67 DUP REM L7 (123 DUPLICATES REMOVED)

=> s 15 and 18

L9 10 L5 AND L8

=> d his

(FILE 'HOME' ENTERED AT 14:04:47 ON 04 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:07:00 ON 04 MAR 2004

L1 997 S MONOCARBOXYLATE(W) TRANSPORTER?
L2 8 S SLC16
L3 5 DUP REM L2 (3 DUPLICATES REMOVED)
L4 113 S L1(S) (FAMILY OR SUPERFAMILY)
L5 40 DUP REM L4 (73 DUPLICATES REMOVED)
L6 214 S MCT4 OR MCT!4
L7 190 S L6 AND L1
L8 67 DUP REM L7 (123 DUPLICATES REMOVED)
L9 10 S L5 AND L8

=> d ibib abs 1-10

L9 ANSWER 1 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2004068746 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12739169
TITLE: The SLC16 gene **family**-from
monocarboxylate transporters (MCTs) to
aromatic amino acid transporters and beyond.
AUTHOR: Halestrap Andrew P; Meredith David
CORPORATE SOURCE: Department of Biochemistry, University of Bristol, BS8 1TD,
Bristol, UK, . A.Halestrap@Bristol.ac.uk
SOURCE: Pflugers Archiv : European journal of physiology, (2004
Feb) 447 (5) 619-28.
Journal code: 0154720. ISSN: 0031-6768.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040211
Last Updated on STN: 20040211

AB The monocarboxylate cotransporter (MCT) family now comprises 14 members, of which only the first four (MCT1-MCT4) have been demonstrated experimentally to catalyse the proton-linked transport of metabolically important monocarboxylates such as lactate, pyruvate and ketone bodies. SLC16A10 (T-type amino-acid transporter-1, TAT1) is an aromatic amino acid transporter whilst the other members await characterization. MCTs have 12 transmembrane domains (TMDs) with intracellular N- and C-termini and a large intracellular loop between TMDs 6 and 7. MCT1 and **MCT4** require a monotopic ancillary protein, CD147, for expression of functional protein at the plasma membrane. Lactic acid transport across the plasma membrane is fundamental for the metabolism of and pH regulation of all cells, removing lactic acid produced by glycolysis and allowing uptake by those cells utilizing it for gluconeogenesis (liver and kidney) or as a respiratory fuel (heart and red muscle). The properties of the different MCT isoforms and their tissue distribution and regulation reflect these roles.

L9 ANSWER 2 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2003351262 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12884241

TITLE: Molecular features, regulation, and function of
monocarboxylate transporters:
implications for drug delivery.

AUTHOR: Enerson Bradley E; Drewes Lester R

CORPORATE SOURCE: School of Medicine Duluth, Biochemistry and Molecular
Biology, 10 University Drive, Duluth, Minnesota 55812, USA.

SOURCE: Journal of pharmaceutical sciences, (2003 Aug) 92 (8)
1531-44.
Journal code: 2985195R. ISSN: 0022-3549.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20030729
Last Updated on STN: 20031218

AB The diffusion of monocarboxylates such as lactate and pyruvate across the plasma membrane of mammalian cells is facilitated by a **family** of integral membrane transport proteins, the **monocarboxylate transporters** (MCTs). Currently, at least eight unique members of the MCT family have been discovered and orthologs to each have been identified in a variety of species. Four MCTs (MCT1-MCT4) have been functionally characterized. Each isoform possesses unique biochemical properties such as kinetic constants and sensitivity to known MCT inhibitors. Several fold changes in the expression of MCTs may be evoked by altered physiological conditions, yet the molecular mechanisms underlying the regulation of MCTs are poorly understood. Post-translational regulation of MCT1 and **MCT4** occurs, in part, by interaction with CD147, an accessory protein that is necessary for trafficking, localization, and functional expression of these transporters. Because of the physiological importance of monocarboxylates to the overall maintenance of metabolic homeostasis, the function of MCTs is significant to several pathologies that occur with disease, such as ischemic stroke and cancer. Finally, the expression of MCT1 in the epithelium of the small intestine and colon and in the blood-brain barrier may provide routes for the intestinal and blood to brain transfer of carboxylated pharmaceutical agents and other exogenous monocarboxylates. Copyright 2003 Wiley-Liss, Inc.

L9 ANSWER 3 OF 10 MEDLINE on STN

ACCESSION NUMBER: 2002486536 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12297728

TITLE: Functional and molecular characterisation of lactic acid transport in bovine articular chondrocytes.

AUTHOR: Meredith David; Bell Peter; McClure Brendan; Wilkins Robert

CORPORATE SOURCE: Department of Human Anatomy and Genetics, University of Oxford, Great Britain.. david.meredith@anat.ox.ac.uk

SOURCE: Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology, (2002) 12 (4) 227-34.
Journal code: 9113221. ISSN: 1015-8987.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 20020926
Last Updated on STN: 20030331
Entered Medline: 20030328

AB Chondrocytes, which control the turnover of cartilage, undergo predominantly glycolytic metabolism due to the avascular nature of the tissue. This will result in high levels of lactic acid production, and

this lactic acid must leave the cells for their normal intracellular pH to be maintained. However to date the mechanism by which lactic acid is removed from the chondrocytes has not been elucidated. In the present study lactic acid transport has been characterised using the intracellular pH-sensitive fluorimetric dye BCECF to measure intracellular pH (pH(i)). Addition of extracellular lactic acid-induced an acidification which was sensitive to alpha-cyano-4-hydroxycinnamate (alpha-CHC) and phloretin indicating the involvement of isoform(s) of the **monocarboxylate transporter** (MCT) **family**. The results studies of transport kinetics were consistent with the **MCT4** isoform (K(m) 14.1mM), common to other glycolytic cells. Western blotting confirmed that **MCT4** was the predominantly expressed isoform, although both MCT1 and **MCT4** transcripts were present when cells were assayed by RT-PCR. Through effects on pH(i), the activity of this transporter may therefore modify cartilage turnover.

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L9 ANSWER 4 OF 10 MEDLINE on STN

ACCESSION NUMBER: 2002314936 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12056458

TITLE: Genetic expression of **monocarboxylate transporters** during human and murine oocyte maturation and early embryonic development.

AUTHOR: Herubel Francois; El Mouatassim Said; Guerin Pierre; Frydman Rene; Menezo Yves

CORPORATE SOURCE: Laboratoire Marcel Merieux, Lyon, France.

SOURCE: Zygote (Cambridge, England), (2002 May) 10 (2) 175-81.
Journal code: 9309124. ISSN: 0967-1994.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 20020612

Last Updated on STN: 20030304

Entered Medline: 20030303

AB During the early preimplantation of human embryos, pyruvate and lactate, but not glucose, are the preferred energy substrates. Transport of these monocarboxylates is mediated, in mammalian cells, by a **family** of transporters, designated as **monocarboxylate transporters** (MCTs). Human and mouse genetic expression of MCT members 1, 2, 3, 4 and basigin, a chaperone protein of MCT1 and **MCT4**, was qualitatively analysed using the reverse transcription nested polymerase chain reaction (RT-nested PCR) in immature oocytes (germinal vesicle stage; GV), in non-fertilised metaphase II (MII) oocytes and in embryos from 2-cell stage to blastocysts. Transcripts encoding for MCT1 and MCT2 were present, under a polyadenylated form, in the majority of the human and mouse oocytes and early embryos. MCT3 transcripts were not detected in either human or mouse. **MCT4** mRNA was not detected in human oocytes and embryos, but was present in mouse oocytes and embryos. This fact could imply differences in lactate transport and regulation of intracellular pH between human and murine early embryos. Basigin transcripts were present in mouse and human MII oocytes and preimplantation embryos, but were not detected at GV stage. However, using 3' end-specific primers in the RT reaction instead of Oligo(dT)12-18 primers, transcripts encoding for this protein were then detected at GV stage in both species. This result suggests that a regulated polyadenylation process occurs during oocyte maturation for these transcripts. Thus, basigin mRNA can be considered as a marker of oocyte cytoplasmic maturation in human and mouse species.

L9 ANSWER 5 OF 10 MEDLINE on STN

ACCESSION NUMBER: 2001171839 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11272148
TITLE: Expression and distribution of lactate/
monocarboxylate transporter isoforms in
pancreatic islets and the exocrine pancreas.
AUTHOR: Zhao C; Wilson M C; Schuit F; Halestrap A P; Rutter G A
CORPORATE SOURCE: Department of Biochemistry, School of Medical Sciences,
University of Bristol, UK.
SOURCE: Diabetes, (2001 Feb) 50 (2) 361-6.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

AB Transport of lactate across the plasma membrane of pancreatic islet
beta-cells is slow, as described by Sekine et al. (J Biol Chem
269:4895-4902, 1994), which is a feature that may be important for normal
nutrient-induced insulin secretion. Although eight members of the
monocarboxylate transporter (MCT) family have
now been identified, the expression of these isoforms within the exocrine
and endocrine pancreas has not been explored in detail. Using
immunocytochemical analysis of pancreatic sections fixed in situ, we
demonstrated three phenomena. First, immunoreactivity of the commonly
expressed lactate transporter isoform MCT1 is near zero in both alpha- and
beta-cells but is abundant in the pancreatic acinar cell plasma membrane.
No MCT2 or **MCT4** was detected in any pancreatic cell type.
Second, Western analysis of purified beta- and non-beta-cell membranes
revealed undetectable levels of MCT1 and **MCT4**. In derived
beta-cell lines, MCT1 was absent from MIN6 cells and present in low
amounts in INS-1 cell membranes and at high levels in RINm5F cells.
MCT4 was weakly expressed in MIN6 beta-cells. Third, CD147, an
MCT-associated chaperone protein, which is closely colocalized with MCT1
on acinar cell membranes, was absent from islet cell membranes. CD147 was
also largely absent from MIN6 and INS-1 cells but abundant in RINm5F
cells. Low expression of MCT1, MCT2, and **MCT4** contributes to
the enzymatic configuration of beta-cells, which is poised to ensure
glucose oxidation and the generation of metabolic signals and may also be
important for glucose sensing in islet non-beta-cells. MCT overexpression
throughout the islet could contribute to deranged hormone secretion in
some forms of type 2 diabetes.

L9 ANSWER 6 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2001080520 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10926847
TITLE: The low-affinity **monocarboxylate**
transporter MCT4 is adapted to the export
of lactate in highly glycolytic cells.
AUTHOR: Dimmer K S; Friedrich B; Lang F; Deitmer J W; Broer S
CORPORATE SOURCE: Physiologisches Institut der Universitat, Gmelinstr. 5,
D-72076 Tübingen, Germany.
SOURCE: Biochemical journal, (2000 Aug 15) 350 Pt 1 219-27.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB Transport of lactate and other monocarboxylates in mammalian cells is mediated by a **family** of transporters, designated **monocarboxylate transporters** (MCTs). The **MCT4** member of this family has recently been identified as the major isoform of white muscle cells, mediating lactate efflux out of glycolytically active myocytes [Wilson, Jackson, Heddle, Price, Pilegaard, Juel, Bonen, Montgomery, Hutter and Halestrap (1998) J. Biol. Chemical 273, 15920-15926]. To analyse the functional properties of this transporter, rat **MCT4** was expressed in *Xenopus laevis* oocytes and transport activity was monitored by flux measurements with radioactive tracers and by changes of the cytosolic pH using pH-sensitive microelectrodes. Similar to other members of this family, monocarboxylate transport via **MCT4** is accompanied by the transport of H(+) across the plasma membrane. Uptake of lactate strongly increased with decreasing extracellular pH, which resulted from a concomitant drop in the K(m) value. **MCT4** could be distinguished from the other isoforms mainly in two respects. First, **MCT4** is a low-affinity MCT: for L-lactate K(m) values of 17+/-3 mM (pH-electrode) and 34+/-5 mM (flux measurements with L-[U-(14)C]lactate) were determined. Secondly, lactate is the preferred substrate of **MCT4**. K(m) values of other monocarboxylates were either similar to the K(m) value for lactate (pyruvate, 2-oxoisohexanoate, 2-oxoisopentanoate, acetoacetate) or displayed much lower affinity for the transporter (beta-hydroxybutyrate and short-chain fatty acids). Under physiological conditions, rat MCT will therefore preferentially transport lactate. Monocarboxylate transport via **MCT4** could be competitively inhibited by alpha-cyano-4-hydroxycinnamate, phloretin and partly by 4, 4'-di-isothiocyanostilbene-2,2'-disulphonic acid. Similar to MCT1, monocarboxylate transport via **MCT4** was sensitive to inhibition by the thiol reagent p-chloromercuribenzoatesulphonic acid.

L9 ANSWER 7 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2001020647 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11005765
TITLE: Mechanism(s) of butyrate transport in Caco-2 cells: role of **monocarboxylate transporter 1**.
AUTHOR: Hadjiagapiou C; Schmidt L; Dudeja P K; Layden T J; Ramaswamy K
CORPORATE SOURCE: Section of Digestive and Liver Diseases, Department of Medicine, University of Illinois at Chicago and the West Side Veterans Affairs Medical Center, Chicago, Illinois 60612, USA.
CONTRACT NUMBER: DK-33349 (NIDDK)
DK-54016 (NIDDK)
SOURCE: American journal of physiology. Gastrointestinal and liver physiology, (2000 Oct) 279 (4) G775-80.
Journal code: 100901227. ISSN: 0193-1857.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20030319
Entered Medline: 20001106

AB The short-chain fatty acid butyrate was readily taken up by Caco-2 cells. Transport exhibited saturation kinetics, was enhanced by low extracellular pH, and was Na(+) independent. Butyrate uptake was unaffected by DIDS;

however, alpha-cyano-4-hydroxycinnamate and the butyrate analogs propionate and L-lactate significantly inhibited uptake. These results suggest that butyrate transport by Caco-2 cells is mediated by a transporter belonging to the **monocarboxylate transporter family**. We identified five isoforms of this transporter, MCT1, MCT3, **MCT4**, MCT5, and MCT6, in Caco-2 cells by PCR, and MCT1 was found to be the most abundant isoform by RNase protection assay. Transient transfection of MCT1, in the antisense orientation, resulted in significant inhibition of butyrate uptake. The cells fully recovered from this inhibition by 5 days after transfection. In conclusion, our data showed that the MCT1 transporter may play a major role in the transport of butyrate into Caco-2 cells.

L9 ANSWER 8 OF 10 MEDLINE on STN
 ACCESSION NUMBER: 1999441227 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10510291
 TITLE: The proton-linked **monocarboxylate transporter** (MCT) **family**: structure, function and regulation.
 AUTHOR: Halestrap A P; Price N T
 CORPORATE SOURCE: Department of Biochemistry, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, U.K..
 A.Halestrap@Bristol.ac.uk
 SOURCE: Biochemical journal, (1999 Oct 15) 343 Pt 2 281-99. Ref: 170
 Journal code: 2984726R. ISSN: 0264-6021.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, ACADEMIC)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199912
 ENTRY DATE: Entered STN: 20000113
 Last Updated on STN: 20000113
 Entered Medline: 19991221

AB Monocarboxylates such as lactate and pyruvate play a central role in cellular metabolism and metabolic communication between tissues. Essential to these roles is their rapid transport across the plasma membrane, which is catalysed by a recently identified **family** of proton-linked **monocarboxylate transporters** (MCTs). Nine MCT-related sequences have so far been identified in mammals, each having a different tissue distribution, whereas six related proteins can be recognized in *Caenorhabditis elegans* and 4 in *Saccharomyces cerevisiae*. Direct demonstration of proton-linked lactate and pyruvate transport has been demonstrated for mammalian MCT1-**MCT4**, but only for MCT1 and MCT2 have detailed analyses of substrate and inhibitor kinetics been described following heterologous expression in *Xenopus* oocytes. MCT1 is ubiquitously expressed, but is especially prominent in heart and red muscle, where it is up-regulated in response to increased work, suggesting a special role in lactic acid oxidation. By contrast, **MCT4** is most evident in white muscle and other cells with a high glycolytic rate, such as tumour cells and white blood cells, suggesting it is expressed where lactic acid efflux predominates. MCT2 has a ten-fold higher affinity for substrates than MCT1 and **MCT4** and is found in cells where rapid uptake at low substrate concentrations may be required, including the proximal kidney tubules, neurons and sperm tails. MCT3 is uniquely expressed in the retinal pigment epithelium. The mechanisms involved in regulating the expression of different MCT isoforms remain to be established. However, there is evidence for alternative splicing of the 5'- and 3'-untranslated regions and the use of alternative promoters

for some isoforms. In addition, MCT1 and **MCT4** have been shown to interact specifically with OX-47 (CD147), a member of the immunoglobulin superfamily with a single transmembrane helix. This interaction appears to assist MCT expression at the cell surface. There is still much work to be done to characterize the properties of the different isoforms and their regulation, which may have wide-ranging implications for health and disease. In the future it will be interesting to explore the linkage of genetic diseases to particular MCTs through their chromosomal location.

L9 ANSWER 9 OF 10 MEDLINE on STN

ACCESSION NUMBER: 1998087501 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9425115

TITLE: Cloning and sequencing of four new mammalian **monocarboxylate transporter** (MCT) homologues confirms the existence of a transporter **family** with an ancient past.

AUTHOR: Price N T; Jackson V N; Halestrap A P

CORPORATE SOURCE: Department of Biochemistry, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, U.K.

SOURCE: Biochemical journal, (1998 Jan 15) 329 (Pt 2) 321-8.
Journal code: 2984726R. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U59299; GENBANK-U79745; GENBANK-U81800

ENTRY MONTH: 199802

ENTRY DATE: Entered STN: 19980306

Last Updated on STN: 20000303

Entered Medline: 19980220

AB Measurement of monocarboxylate transport kinetics in a range of cell types has provided strong circumstantial evidence for a **family** of **monocarboxylate transporters** (MCTs). Two mammalian MCT isoforms (MCT1 and MCT2) and a chicken isoform (REMP or MCT3) have already been cloned, sequenced and expressed, and another MCT-like sequence (XPCT) has been identified. Here we report the identification of new human MCT homologues in the database of expression sequence tags and the cloning and sequencing of four new full-length MCT-like sequences from human cDNA libraries, which we have denoted MCT3, **MCT4**, MCT5 and MCT6. Northern blotting revealed a unique tissue distribution for the expression of mRNA for each of the seven putative MCT isoforms (MCT1-MCT6 and XPCT). All sequences were predicted to have 12 transmembrane (TM) helical domains with a large intracellular loop between TM6 and TM7. Multiple sequence alignments showed identities ranging from 20% to 55%, with the greatest conservation in the predicted TM regions and more variation in the C-terminal than the N-terminal region. Searching of additional sequence databases identified candidate MCT homologues from the yeast *Saccharomyces cerevisiae*, the nematode worm *Caenorhabditis elegans* and the archaeobacterium *Sulfolobus solfataricus*. Together these sequences constitute a new family of transporters with some strongly conserved sequence motifs, the possible functions of which are discussed.

L9 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:154598 BIOSIS

DOCUMENT NUMBER: PREV200300154598

TITLE: Expression and Polarity of **Monocarboxylate Transporters** in Human Retinal Pigment Epithelium.

AUTHOR(S): Philp, N. J. [Reprint Author]; Yoon, H. [Reprint Author]; Wang, D. [Reprint Author]

CORPORATE SOURCE: Pathology, Anatomy and Cell Biology, Thomas Jefferson

SOURCE: University, Philadelphia, PA, USA
 ARVO Annual Meeting Abstract Search and Program Planner,
 (2002) Vol. 2002, pp. Abstract No. 2428. cd-rom.
 Meeting Info.: Annual Meeting of the Association For
 Research in Vision and Ophthalmology. Fort Lauderdale,
 Florida, USA. May 05-10, 2002.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Mar 2003
 Last Updated on STN: 26 Mar 2003

AB Purpose: To identify the **monocarboxylate transporters** (MCTs) expressed in human retinal pigment epithelium (RPE) in situ and in ARPE-19 cells. Methods: MCT expression in human RPE and ARPE-19 cells was determined using reverse transcription-polymerase chain reaction (RT-PCR) with isoform specific primers. Immunohistochemical localization of MCTs in human donor eyes and ARPE-19 cells was performed using isoform specific peptide antibodies. Specificity of antibodies was determined by Western blot analysis. Results: MCT1 and MCT3 were amplified by RT-PCR from RPE-choroid complex and differentiated ARPE-19 cells. While most cells express MCT1, we previously showed in mouse that MCT3 is preferentially expressed by the RPE. Immunofluorescence microscopy of adult human donor eye revealed a polarized distribution of MCTs in the RPE. MCT1 antibody labeled the apical membrane of the RPE while labeling with MCT3 antibodies was restricted to the basolateral surface. Similarly, immuno-labeling of sections through differentiated ARPE-19 cell cultures showed that MCT1 was polarized to the apical membrane. There was no detectable MCT3 labeling in ARPE-19 cells even though the transcript was expressed. ARPE-19 cells expressed **MCT4**, a MCT isoform closely related to MCT3. Immunohistochemical labeling of ARPE-19 cells with antibodies specific for **MCT4** demonstrated selective labeling of the basolateral membrane. While the RPE cells express two MCT isoforms, only one glucose transporter is expressed, GLUT1. GLUT1 antibody labeled the apical and basolateral membranes of human RPE and ARPE-19 cells. Conclusion: **Monocarboxylate transporters** (MCTs) are a family of highly homologous membrane proteins that mediate the 1:1 transport of a proton and a lactate ion. Lactate is both an end product and a substrate of energy metabolism in the retina. The expression two distinct MCT isoforms in RPE is consistent with a role for the RPE in regulating lactate levels in the outer retina. The coordinated activities of MCT1 in the apical membrane and MCT3 in the basolateral membrane could control transepithelial movement of lactate.

=> d his

(FILE 'HOME' ENTERED AT 14:04:47 ON 04 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:07:00 ON 04 MAR 2004

L1 997 S MONOCARBOXYLATE(W)TRANSPORTER?
 L2 8 S SLC16
 L3 5 DUP REM L2 (3 DUPLICATES REMOVED)
 L4 113 S L1(S) (FAMILY OR SUPERFAMILY)
 L5 40 DUP REM L4 (73 DUPLICATES REMOVED)
 L6 214 S MCT4 OR MCT!4
 L7 190 S L6 AND L1
 L8 67 DUP REM L7 (123 DUPLICATES REMOVED)
 L9 10 S L5 AND L8

=> s l5 and (function? or activit?)

L10 19 L5 AND (FUNCTION? OR ACTIVIT?)

=> d ibib abs 1-19

L10 ANSWER 1 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2004068746 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12739169
TITLE: The SLC16 gene **family**-from
monocarboxylate transporters (MCTs) to
aromatic amino acid transporters and beyond.
AUTHOR: Halestrap Andrew P; Meredith David
CORPORATE SOURCE: Department of Biochemistry, University of Bristol, BS8 1TD,
Bristol, UK, . A.Halestrap@Bristol.ac.uk
SOURCE: Pflugers Archiv : European journal of physiology, (2004
Feb) 447 (5) 619-28.
Journal code: 0154720. ISSN: 0031-6768.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040211
Last Updated on STN: 20040211

AB The monocarboxylate cotransporter (MCT) family now comprises 14 members,
of which only the first four (MCT1-MCT4) have been demonstrated
experimentally to catalyse the proton-linked transport of metabolically
important monocarboxylates such as lactate, pyruvate and ketone bodies.
SLC16A10 (T-type amino-acid transporter-1, TAT1) is an aromatic amino acid
transporter whilst the other members await characterization. MCTs have 12
transmembrane domains (TMDs) with intracellular N- and C-termini and a
large intracellular loop between TMDs 6 and 7. MCT1 and MCT4 require a
monotopic ancillary protein, CD147, for expression of **functional**
protein at the plasma membrane. Lactic acid transport across the plasma
membrane is fundamental for the metabolism of and pH regulation of all
cells, removing lactic acid produced by glycolysis and allowing uptake by
those cells utilizing it for gluconeogenesis (liver and kidney) or as a
respiratory fuel (heart and red muscle). The properties of the different
MCT isoforms and their tissue distribution and regulation reflect these
roles.

L10 ANSWER 2 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003548466 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12946269
TITLE: The loop between helix 4 and helix 5 in the monocarboxylate
transporter MCT1 is important for substrate selection and
protein stability.
AUTHOR: Galic Sandra; Schneider Hans-Peter; Broer Angelika; Deitmer
Joachim W; Broer Stefan
CORPORATE SOURCE: School of Biochemistry & Molecular Biology, Australian
National University, Canberra ACT 0200, Australia.
SOURCE: Biochemical journal, (2003 Dec 1) 376 (Pt 2) 413-22.
Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031121
Last Updated on STN: 20031219
Entered Medline: 20031202

AB Transport of lactate, pyruvate and the ketone bodies acetoacetate and
beta-hydroxybutyrate, is mediated in most mammalian cells by members of

the **monocarboxylate transporter family**

(SLC16). A conserved signature sequence has been identified in this family, which is located in the loop between helix 4 and helix 5 and extends into helix 5. We have mutated residues in this signature sequence in the rat monocarboxylate transporter (MCT1) to elucidate the significance of this region for monocarboxylate transport. Mutation of R143 and G153 resulted in complete inactivation of the transporter. For the MCT1(G153V) mutant this was explained by a failure to reach the plasma membrane. The lack of transport **activity** of MCT1(R143Q) could be partially rescued by the conservative exchange R143H. The resulting mutant transporter displayed reduced stability, a decreased V_{max} of lactate transport but not of acetate transport, and an increased stereoselectivity. Mutation of K137, K141 and K142 indicated that only K142 played a significant role in the transport mechanism. Mutation of K142 to glutamine resulted in an increase of the K_m for lactate from 5 mM to 12 mM. In contrast with MCT1(R143H), MCT1(K142Q) was less stereoselective than the wild-type. A mechanism is proposed that includes all critical residues.

L10 ANSWER 3 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003508963 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14585264
TITLE: Cellular pH regulators: potentially promising molecular targets for cancer chemotherapy.
AUTHOR: Izumi Hiroto; Torigoe Takayuki; Ishiguchi Hiroshi; Uramoto Hidetaka; Yoshida Yoichiro; Tanabe Mizuho; Ise Tomoko; Murakami Tadashi; Yoshida Takeshi; Nomoto Minoru; Kohno Kimitoshi
CORPORATE SOURCE: Department of Molecular Biology, University of Occupational and Environmental Health, School of medicine, Fukuoka 807-8555, Japan.
SOURCE: Cancer treatment reviews, (2003 Dec) 29 (6) 541-9. Ref: 62
Journal code: 7502030. ISSN: 0305-7372.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031031
Last Updated on STN: 20031219
Entered Medline: 20031126

AB One of the major obstacles to the successful treatment of cancer is the complex biology of solid tumour development. Although regulation of intracellular pH has been shown to be critically important for many cellular **functions**, pH regulation has not been fully investigated in the field of cancer. It has, however, been shown that cellular pH is crucial for biological **functions** such as cell proliferation, invasion and metastasis, drug resistance and apoptosis. Hypoxic conditions are often observed during the development of solid tumours and lead to intracellular and extracellular acidosis. Cellular acidosis has been shown to be a trigger in the early phase of apoptosis and leads to activation of endonucleases inducing DNA fragmentation. To avoid intracellular acidification under such conditions, pH regulators are thought to be up-regulated in tumour cells. Four major types of pH regulator have been identified: the proton pump, the sodium-proton exchanger **family** (NHE), the bicarbonate transporter **family** (BCT) and the **monocarboxylate transporter family** (MCT). Here, we describe the structure and **function** of pH regulators expressed in tumour tissue.

Understanding pH regulation in tumour cells may provide new ways of inducing tumour-specific apoptosis, thus aiding cancer chemotherapy.

L10 ANSWER 4 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003479872 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12969152
TITLE: Regulation of cytosolic pH and lactic acid release in mesangial cells overexpressing GLUT1.
AUTHOR: Lang Karl S; Mueller Matthias M; Tanneur Valerie; Wallisch Sabine; Fedorenko Olga; Palmada Monica; Lang Florian; Broer Stefan; Heilig Charles W; Schleicher Erwin; Weigert Cora
CORPORATE SOURCE: Department of Physiology, University of Tübingen, Tübingen, Germany.
SOURCE: Kidney international, (2003 Oct) 64 (4) 1338-47.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20031016
Last Updated on STN: 20031219

AB BACKGROUND: Anaerobic glycolysis leads to the formation of lactate and H⁺ and thus imposes a significant challenge on cytosolic acid/base regulation. Cytosolic acidification, on the other hand, is known to inhibit flux through glycolysis and lactate formation. To explore the interplay of cytosolic pH and glycolysis, rat mesangial cells transfected with the glucose transporter GLUT1 (GLUT1 cells) were compared with those transfected with beta-galactosidase (LacZ cells). METHODS: In the presence of extracellular glucose, the glycolytic rate was one order of magnitude higher in GLUT1 cells than in LacZ cells. Cytosolic pH (pHi) was significantly higher in GLUT1 than LacZ cells, an effect abolished in the presence of Na⁺/H⁺ exchange inhibitor ethylisopropylamiloride (1 micromol/L). RESULTS: Addition of 40 mmol/L lactate led to marked cytosolic acidification, which was in both cell types blunted by O-methyl-glucose (20 mmol/L) and completely abolished by 100 micromol/L phloretin and 1 mmol/L p-chloromercuribenzenesulphonic acid (p-CMBS) and in LacZ cells only by glucose (20 mmol/L). The **functional** characterization points to the involvement of a lactic acid transporter from the **monocarboxylate transporter (MCT)** family, particularly MCT1. Reverse transcription-polymerase chain reaction (RT-PCR) indeed disclosed the expression of MCT1 and MCT2 in both GLUT1 and LacZ cells. CONCLUSION: Overexpression of GLUT1 leads to cytosolic alkalization of mesangial cells depending on **functional** Na⁺/H⁺ exchanger but not on Na⁺ independent H⁺ transport.

L10 ANSWER 5 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003351262 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12884241
TITLE: Molecular features, regulation, and **function** of monocarboxylate transporters: implications for drug delivery.
AUTHOR: Enerson Bradley E; Drewes Lester R
CORPORATE SOURCE: School of Medicine Duluth, Biochemistry and Molecular Biology, 10 University Drive, Duluth, Minnesota 55812, USA.
SOURCE: Journal of pharmaceutical sciences, (2003 Aug) 92 (8) 1531-44.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030729
Last Updated on STN: 20031218

AB The diffusion of monocarboxylates such as lactate and pyruvate across the plasma membrane of mammalian cells is facilitated by a **family** of integral membrane transport proteins, the **monocarboxylate transporters** (MCTs). Currently, at least eight unique members of the MCT family have been discovered and orthologs to each have been identified in a variety of species. Four MCTs (MCT1-MCT4) have been **functionally** characterized. Each isoform possesses unique biochemical properties such as kinetic constants and sensitivity to known MCT inhibitors. Several fold changes in the expression of MCTs may be evoked by altered physiological conditions, yet the molecular mechanisms underlying the regulation of MCTs are poorly understood. Post-translational regulation of MCT1 and MCT4 occurs, in part, by interaction with CD147, an accessory protein that is necessary for trafficking, localization, and **functional** expression of these transporters. Because of the physiological importance of monocarboxylates to the overall maintenance of metabolic homeostasis, the **function** of MCTs is significant to several pathologies that occur with disease, such as ischemic stroke and cancer. Finally, the expression of MCT1 in the epithelium of the small intestine and colon and in the blood-brain barrier may provide routes for the intestinal and blood to brain transfer of carboxylated pharmaceutical agents and other exogenous monocarboxylates.
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L10 ANSWER 6 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003338272 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 12870677
TITLE: A 44-kDa of protein identical to the N-terminal amino acid sequence of MCT1 in human circulation.
AUTHOR: Iizuka Kenji; Morita Noriteru; Nagai Tatsuya; Hanada Akiko; Okita Koichi; Yonezawa Kazuya; Murakami Takeshi; Kitabatake Akira; Kawaguchi Hideaki
CORPORATE SOURCE: Department of Laboratory Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan..
kiizuka@med.hokudai.ac.jp
SOURCE: Molecular and cellular biochemistry, (2003 Jun) 248 (1-2) 217-23.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030722
Last Updated on STN: 20031218

AB A **family** of specific carrier protein designated as **monocarboxylate transporter** (MCT) has been known to transport the lactate and other monocarboxylates in mammalian cells. We hypothesized the presence of serum protein in human circulation that may works as a lactate carrier and that biochemical structure would possesses common structure with MCT on the plasma membrane. Immunoblot analysis with an anti-MCT1 polyclonal antibody suggested the presence of a 44-kDa protein in human circulation and N-terminal amino acid sequencing exhibited a stretch of 14 amino acids which is completely identical to MCT1. The unbound fractions from the GST-MCT1 fusion protein-immobilized glutathione sepharose 4B column demonstrated that lactic acid concentration began to increase with one fraction delay compared to Sepharose 4B and GST-immobilized column. When lactic acid was washed away with PBS, lactic acid concentrations in the effluent constantly decreased

in both Sepharose 4B and GST-immobilized column. However, GST-MCT1-immobilized column showed specific convex curve from fraction approximately 3 mM of lactate and demonstrated wash out delay compared to Sepharose 4B and GST-immobilized column. These observations demonstrated biochemical and immunological similarities between a 44-kDa protein purified from human serum and MCT1 present on the plasma membrane. The studies on MCT1-fusion protein suggested possible **functional** properties of a 44-kDa protein as a lactate buffer by holding and unhand a lactate according to the lactate concentration in human blood. The experiments described herein have suggested the existence of lactate carrier in human circulation which is free from plasma membrane.

L10 ANSWER 7 OF 19 MEDLINE on STN

ACCESSION NUMBER: 2002486536 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12297728

TITLE: **Functional** and molecular characterisation of lactic acid transport in bovine articular chondrocytes.

AUTHOR: Meredith David; Bell Peter; McClure Brendan; Wilkins Robert

CORPORATE SOURCE: Department of Human Anatomy and Genetics, University of Oxford, Great Britain.. david.meredith@anat.ox.ac.uk

SOURCE: Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology, (2002) 12 (4) 227-34.
Journal code: 9113221. ISSN: 1015-8987.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 20020926

Last Updated on STN: 20030331

Entered Medline: 20030328

AB Chondrocytes, which control the turnover of cartilage, undergo predominantly glycolytic metabolism due to the avascular nature of the tissue. This will result in high levels of lactic acid production, and this lactic acid must leave the cells for their normal intracellular pH to be maintained. However to date the mechanism by which lactic acid is removed from the chondrocytes has not been elucidated. In the present study lactic acid transport has been characterised using the intracellular pH-sensitive fluorimetric dye BCECF to measure intracellular pH (pH(i)). Addition of extracellular lactic acid-induced an acidification which was sensitive to alpha-cyano-4-hydroxycinnamate (alpha-CHC) and phloretin indicating the involvement of isoform(s) of the **monocarboxylate transporter (MCT) family**. The results studies of transport kinetics were consistent with the MCT4 isoform (K(m) 14.1mM), common to other glycolytic cells. Western blotting confirmed that MCT4 was the predominantly expressed isoform, although both MCT1 and MCT4 transcripts were present when cells were assayed by RT-PCR. Through effects on pH(i), the **activity** of this transporter may therefore modify cartilage turnover.

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L10 ANSWER 8 OF 19 MEDLINE on STN

ACCESSION NUMBER: 2001080520 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10926847

TITLE: The low-affinity monocarboxylate transporter MCT4 is adapted to the export of lactate in highly glycolytic cells.

AUTHOR: Dimmer K S; Friedrich B; Lang F; Deitmer J W; Broer S

CORPORATE SOURCE: Physiologisches Institut der Universitat, Gmelinstr. 5, D-72076 Tübingen, Germany.

SOURCE: Biochemical journal, (2000 Aug 15) 350 Pt 1 219-27.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB Transport of lactate and other monocarboxylates in mammalian cells is mediated by a **family** of transporters, designated **monocarboxylate transporters** (MCTs). The MCT4 member of this family has recently been identified as the major isoform of white muscle cells, mediating lactate efflux out of glycolytically active myocytes [Wilson, Jackson, Heddle, Price, Pilegaard, Juel, Bonen, Montgomery, Hutter and Halestrap (1998) J. Biol. Chemical 273, 15920-15926]. To analyse the **functional** properties of this transporter, rat MCT4 was expressed in *Xenopus laevis* oocytes and transport **activity** was monitored by flux measurements with radioactive tracers and by changes of the cytosolic pH using pH-sensitive microelectrodes. Similar to other members of this family, monocarboxylate transport via MCT4 is accompanied by the transport of H(+) across the plasma membrane. Uptake of lactate strongly increased with decreasing extracellular pH, which resulted from a concomitant drop in the K(m) value. MCT4 could be distinguished from the other isoforms mainly in two respects. First, MCT4 is a low-affinity MCT: for L-lactate K(m) values of 17+/-3 mM (pH-electrode) and 34+/-5 mM (flux measurements with L-[U-(14)C]lactate) were determined. Secondly, lactate is the preferred substrate of MCT4. K(m) values of other monocarboxylates were either similar to the K(m) value for lactate (pyruvate, 2-oxoisohexanoate, 2-oxoisopentanoate, acetoacetate) or displayed much lower affinity for the transporter (beta-hydroxybutyrate and short-chain fatty acids). Under physiological conditions, rat MCT will therefore preferentially transport lactate. Monocarboxylate transport via MCT4 could be competitively inhibited by alpha-cyano-4-hydroxycinnamate, phloretin and partly by 4, 4'-di-isothiocyanostilbene-2,2'-disulphonic acid. Similar to MCT1, monocarboxylate transport via MCT4 was sensitive to inhibition by the thiol reagent p-chloromercuribenzoic acid.

L10 ANSWER 9 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1999441227 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10510291
TITLE: The proton-linked **monocarboxylate transporter** (MCT) **family**: structure, **function** and regulation.
AUTHOR: Halestrap A P; Price N T
CORPORATE SOURCE: Department of Biochemistry, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, U.K..
A.Halestrap@Bristol.ac.uk
SOURCE: Biochemical journal, (1999 Oct 15) 343 Pt 2 281-99. Ref: 170
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113

Last Updated on STN: 20000113

Entered Medline: 19991221

AB Monocarboxylates such as lactate and pyruvate play a central role in cellular metabolism and metabolic communication between tissues. Essential to these roles is their rapid transport across the plasma membrane, which is catalysed by a recently identified **family** of proton-linked **monocarboxylate transporters** (MCTs). Nine MCT-related sequences have so far been identified in mammals, each having a different tissue distribution, whereas six related proteins can be recognized in *Caenorhabditis elegans* and 4 in *Saccharomyces cerevisiae*. Direct demonstration of proton-linked lactate and pyruvate transport has been demonstrated for mammalian MCT1-MCT4, but only for MCT1 and MCT2 have detailed analyses of substrate and inhibitor kinetics been described following heterologous expression in *Xenopus* oocytes. MCT1 is ubiquitously expressed, but is especially prominent in heart and red muscle, where it is up-regulated in response to increased work, suggesting a special role in lactic acid oxidation. By contrast, MCT4 is most evident in white muscle and other cells with a high glycolytic rate, such as tumour cells and white blood cells, suggesting it is expressed where lactic acid efflux predominates. MCT2 has a ten-fold higher affinity for substrates than MCT1 and MCT4 and is found in cells where rapid uptake at low substrate concentrations may be required, including the proximal kidney tubules, neurons and sperm tails. MCT3 is uniquely expressed in the retinal pigment epithelium. The mechanisms involved in regulating the expression of different MCT isoforms remain to be established. However, there is evidence for alternative splicing of the 5'- and 3'-untranslated regions and the use of alternative promoters for some isoforms. In addition, MCT1 and MCT4 have been shown to interact specifically with OX-47 (CD147), a member of the immunoglobulin superfamily with a single transmembrane helix. This interaction appears to assist MCT expression at the cell surface. There is still much work to be done to characterize the properties of the different isoforms and their regulation, which may have wide-ranging implications for health and disease. In the future it will be interesting to explore the linkage of genetic diseases to particular MCTs through their chromosomal location.

L10 ANSWER 10 OF 19 MEDLINE on STN

ACCESSION NUMBER: 1998400885 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9725820

TITLE: Monocarboxylate transporter expression in mouse brain.

AUTHOR: Koehler-Stec E M; Simpson I A; Vannucci S J; Landschulz K T; Landschulz W H

CORPORATE SOURCE: Experimental Diabetes, Metabolism and Nutrition Section, Diabetes Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.

CONTRACT NUMBER: HD-31521 (NICHD)

SOURCE: American journal of physiology, (1998 Sep) 275 (3 Pt 1) E516-24.

Journal code: 0370511. ISSN: 0002-9513.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 19981020

Last Updated on STN: 19981020

Entered Medline: 19981005

AB Although glucose is the major metabolic fuel needed for normal brain **function**, monocarboxylic acids, i.e., lactate, pyruvate, and ketone bodies, can also be utilized by the brain as alternative energy

substrates. In most mammalian cells, these substrates are transported either into or out of the cell by a **family** of **monocarboxylate transporters** (MCTs), first cloned and sequenced in the hamster. We have recently cloned two MCT isoforms (MCT1 and MCT2) from a mouse kidney cDNA library. Northern blot analysis revealed that MCT1 mRNA is ubiquitous and can be detected in most tissues at a relatively constant level. MCT2 expression is more limited, with high levels of expression confined to testes, kidney, stomach, and liver and lower levels in lung, brain, and epididymal fat. Both MCT1 mRNA and MCT2 mRNA are detected in mouse brain using antisense riboprobes and in situ hybridization. MCT1 mRNA is found throughout the cortex, with higher levels of hybridization in hippocampus and cerebellum. MCT2 mRNA was detected in the same areas, but the pattern of expression was more specific. In addition, MCT1 mRNA, but not MCT2, is localized to the choroid plexus, ependyma, microvessels, and white matter structures such as the corpus callosum. These results suggest a differential expression of the two MCTs at the cellular level.

L10 ANSWER 11 OF 19 MEDLINE on STN

ACCESSION NUMBER: 1998087501 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9425115

TITLE: Cloning and sequencing of four new mammalian **monocarboxylate transporter** (MCT) homologues confirms the existence of a transporter **family** with an ancient past.

AUTHOR: Price N T; Jackson V N; Halestrap A P

CORPORATE SOURCE: Department of Biochemistry, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, U.K.

SOURCE: Biochemical journal, (1998 Jan 15) 329 (Pt 2) 321-8.
Journal code: 2984726R. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U59299; GENBANK-U79745; GENBANK-U81800

ENTRY MONTH: 199802

ENTRY DATE: Entered STN: 19980306

Last Updated on STN: 20000303

Entered Medline: 19980220

AB Measurement of monocarboxylate transport kinetics in a range of cell types has provided strong circumstantial evidence for a **family** of **monocarboxylate transporters** (MCTs). Two mammalian MCT isoforms (MCT1 and MCT2) and a chicken isoform (REMP or MCT3) have already been cloned, sequenced and expressed, and another MCT-like sequence (XPCT) has been identified. Here we report the identification of new human MCT homologues in the database of expression sequence tags and the cloning and sequencing of four new full-length MCT-like sequences from human cDNA libraries, which we have denoted MCT3, MCT4, MCT5 and MCT6. Northern blotting revealed a unique tissue distribution for the expression of mRNA for each of the seven putative MCT isoforms (MCT1-MCT6 and XPCT). All sequences were predicted to have 12 transmembrane (TM) helical domains with a large intracellular loop between TM6 and TM7. Multiple sequence alignments showed identities ranging from 20% to 55%, with the greatest conservation in the predicted TM regions and more variation in the C-terminal than the N-terminal region. Searching of additional sequence databases identified candidate MCT homologues from the yeast *Saccharomyces cerevisiae*, the nematode worm *Caenorhabditis elegans* and the archaeobacterium *Sulfolobus solfataricus*. Together these sequences constitute a new family of transporters with some strongly conserved sequence motifs, the possible **functions** of which are discussed.

L10 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:20274 CAPLUS

DOCUMENT NUMBER: 136:397373

TITLE: Advances in study of the **monocarboxylate transporter (MCT) gene family**

AUTHOR(S): Zhang, Guizhi; Huang, Guijun; Guo, Xianjian

CORPORATE SOURCE: Institute of Respiratory Disease, Xinqiao Hospital, Third Military Medical University, Chungking, 400037, Peop. Rep. China

SOURCE: Shengwu Huaxue Yu Shengwu Wuli Jinzhan (2001), 28(2), 172-174

CODEN: SHYCD4; ISSN: 1000-3282

PUBLISHER: Shengwu Huaxue Yu Shengwu Wuli Jinzhan Bianjibu

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB A review with 18 refs. on the **monocarboxylate transporter gene family** including structure, **function**, tissue distribution, and regulation of MCT gene **family** expression.

L10 ANSWER 13 OF 19 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:154598 BIOSIS

DOCUMENT NUMBER: PREV200300154598

TITLE: Expression and Polarity of Monocarboxylate Transporters in Human Retinal Pigment Epithelium.

AUTHOR(S): Philp, N. J. [Reprint Author]; Yoon, H. [Reprint Author]; Wang, D. [Reprint Author]

CORPORATE SOURCE: Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA, USA

SOURCE: ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 2428. cd-rom. Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Mar 2003

Last Updated on STN: 26 Mar 2003

AB Purpose: To identify the monocarboxylate transporters (MCTs) expressed in human retinal pigment epithelium (RPE) in situ and in ARPE-19 cells. Methods: MCT expression in human RPE and ARPE-19 cells was determined using reverse transcription-polymerase chain reaction (RT-PCR) with isoform specific primers. Immunohistochemical localization of MCTs in human donor eyes and ARPE-19 cells was performed using isoform specific peptide antibodies. Specificity of antibodies was determined by Western blot analysis. Results: MCT1 and MCT3 were amplified by RT-PCR from RPE-choroid complex and differentiated ARPE-19 cells. While most cells express MCT1, we previously showed in mouse that MCT3 is preferentially expressed by the RPE. Immunofluorescence microscopy of adult human donor eye revealed a polarized distribution of MCTs in the RPE. MCT1 antibody labeled the apical membrane of the RPE while labeling with MCT3 antibodies was restricted to the basolateral surface. Similarly, immuno-labeling of sections through differentiated ARPE-19 cell cultures showed that MCT1 was polarized to the apical membrane. There was no detectable MCT3 labeling in ARPE-19 cells even though the transcript was expressed. ARPE-19 cells expressed MCT4, a MCT isoform closely related to MCT3. Immunohistochemical labeling of ARPE-19 cells with antibodies specific for MCT4 demonstrated selective labeling of the basolateral membrane. While the RPE cells express two MCT isoforms, only one glucose transporter is expressed, GLUT1. GLUT1 antibody labeled the apical and basolateral

membranes of human RPE and ARPE-19 cells. Conclusion:

Monocarboxylate transporters (MCTs) are a **family** of highly homologous membrane proteins that mediate the 1:1 transport of a proton and a lactate ion. Lactate is both an end product and a substrate of energy metabolism in the retina. The expression two distinct MCT isoforms in RPE is consistent with a role for the RPE in regulating lactate levels in the outer retina. The coordinated **activities** of MCT1 in the apical membrane and MCT3 in the basolateral membrane could control transepithelial movement of lactate.

L10 ANSWER 14 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2004:10980 SCISEARCH

THE GENUINE ARTICLE: 753UY

TITLE: The loop between helix 4 and helix 5 in the monocarboxylate transporter MCT1 is important for substrate selection and protein stability

AUTHOR: Galic S; Schneider H P; Broer A; Deitmer J W; Broer S (Reprint)

CORPORATE SOURCE: Australian Natl Univ, Sch Biochem & Mol Biol, Canberra, ACT 0200, Australia (Reprint); Univ Kaiserslautern, FB Biol, Abt Allgemeine Zool, D-67653 Kaiserslautern, Germany

COUNTRY OF AUTHOR: Australia; Germany

SOURCE: BIOCHEMICAL JOURNAL, (1 DEC 2003) Vol. 376, Part 2, pp. 413-422.

Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND.

ISSN: 0264-6021.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transport of lactate, pyruvate and the ketone bodies acetoacetate and beta-hydroxybutyrate, is mediated in most mammalian cells by members of the **monocarboxylate transporter family** (SLC16). A conserved signature sequence has been identified in this **family**, which is located in the loop between helix 4 and helix 5 and extends into helix 5. We have mutated residues in this signature sequence in the rat **monocarboxylate transporter** (MCT1) to elucidate the significance of this region for monocarboxylate transport. Mutation of R143 and G153 resulted in complete inactivation of the transporter. For the MCT1(G153V) mutant this was explained by a failure to reach the plasma membrane. The lack of transport **activity** of MCT1(R143Q) could be partially rescued by the conservative exchange R143H. The resulting mutant transporter displayed reduced stability, a decreased V-max of lactate transport but not of acetate transport, and an increased stereoselectivity. Mutation of K137, K141 and K142 indicated that only K142 played a significant role in the transport mechanism. Mutation of K142 to glutamine resulted in an increase of the Km for lactate from 5 mM to 12 mM. In contrast with MCT1(R143H), MCT1(K142Q) was less stereoselective than the wild-type. A mechanism is proposed that includes all critical residues.

L10 ANSWER 15 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2002:269665 SCISEARCH

THE GENUINE ARTICLE: 534ME

TITLE: Aluminum citrate uptake by immortalized brain endothelial cells: implications for its blood-brain barrier transport

AUTHOR: Yokel R A (Reprint); Wilson M; Harris W R; Halestrap A P

CORPORATE SOURCE: Univ Kentucky, Med Ctr, Coll Pharm, 501B Pharm Bldg Rose St, Lexington, KY 40536 USA (Reprint); Univ Kentucky, Med Ctr, Coll Pharm, Lexington, KY 40536 USA; Univ Kentucky,

Med Ctr, Grad Ctr Toxicol, Lexington, KY 40536 USA; Univ
Bristol, Sch Med Sci, Dept Biochem, Bristol BS8 1TD, Avon,
England; Univ Missouri, Dept Chem, St Louis, MO 63121 USA
COUNTRY OF AUTHOR: USA; England
SOURCE: BRAIN RESEARCH, (15 MAR 2002) Vol. 930, No. 1-2, pp.
101-110.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE
AMSTERDAM, NETHERLANDS.
ISSN: 0006-8993.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The objective was to further test the hypothesis that aluminum (Al) citrate transport across the blood-brain barrier is mediated by a **monocarboxylate transporter** (MCT). Speciation calculations showed that Al citrates were the predominant Al species under the conditions employed. Al citrate did not inhibit lactate uptake and was not taken up by the rat erythrocyte, suggesting it does not serve as an effective substrate for either MCT1 or the anion exchanger. Studies were conducted with b.End5 cells derived from mouse brain endothelial cells to identify the properties of the carrier(s) mediating Al citrate transport. Western blot analysis of b.End5 cells showed expression of the transferrin receptor and MCT1, but not MCT2 or MCT4. Uptake of Al citrate was similar to 70% faster than citrate. Citrate and Al citrate uptake were sodium independent. Citrate uptake increased at pH 6.9 compared to 7.4, whereas Al citrate uptake did not. Al citrate uptake was reduced by inhibitors of mitochondrial respiration and oxidative phosphorylation, suggesting ATP dependence, but not by ouabain, suggesting no role for Na/K-ATPase. Uptake was not affected by alpha-ketoglutarate or malonate, substrates for the dicarboxylate carrier. Many substrates and inhibitors of MCT1 and organic anion transporters reduced Al citrate uptake into b.End5 cells. BSP and fluorescein, organic anion transporter substrates /inhibitors, inhibited Al citrate uptake. We conclude that Al citrate transport across the blood-brain barrier is carrier-mediated, involving either an uncharacterized MCT isoform expressed in the brain such as MCT7 or MCT8 and/or one of the many members of the organic anion transporting protein **family**, some of which are known to be expressed at the blood-brain barrier. (C) 2002 Elsevier Science B.V. All rights reserved.

L10 ANSWER 16 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:796337 SCISEARCH
THE GENUINE ARTICLE: 475JP
TITLE: The putative monocarboxylate permeases of the yeast
Saccharomyces cerevisiae do not transport monocarboxylic
acids across the plasma membrane
AUTHOR: Makuc J; Paiva S; Schauen M; Kramer R; Andre B; Casal M;
Leao C; Boles E (Reprint)
CORPORATE SOURCE: Univ Dusseldorf, Inst Mikrobiol, Univ Str 1, D-40225
Dusseldorf, Germany (Reprint); Univ Dusseldorf, Inst
Mikrobiol, D-40225 Dusseldorf, Germany; Univ Minho, Dept
Biol, Ctr Ciencias Ambiente, P-4719 Braga, Portugal; Univ
Cologne, Inst Biochem, D-50674 Cologne, Germany; Free Univ
Brussels, Lab Physiol Cellulaire CP300, IBMM, B-6041
Gosselies, Belgium
COUNTRY OF AUTHOR: Germany; Portugal; Belgium
SOURCE: YEAST, (15 SEP 2001) Vol. 18, No. 12, pp. 1131-1143.
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER,
W SUSSEX PO19 1UD, ENGLAND.
ISSN: 0749-503X.
DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have characterized the monocarboxylate permease **family** of *Saccharomyces cerevisiae* comprising five proteins. We could not find any evidence that the **monocarboxylate transporter**-homologous (Mch) proteins of *S. cerevisiae* are involved in the uptake or secretion of monocarboxylates such as lactate, pyruvate or acetate across the plasma membrane. A yeast mutant strain deleted for all five MCH genes exhibited no growth defects on monocarboxylic acids as the sole carbon and energy sources. Moreover, the uptake and secretion rates of monocarboxylic acids were indistinguishable from the wildtype strain. Additional deletion of the JEN1 lactate transporter gene completely blocked uptake of lactate and pyruvate. However, uptake of acetate was not even affected after the additional deletion of the gene YHL008c, which had been proposed to code for an acetate transporter. The mchl-5 mutant strain showed strongly reduced biomass yields in aerobic glucose-limited chemostat cultures, pointing to the involvement of Mch transporters in mitochondrial metabolism. Indeed, intracellular localization studies indicated that at least some of the Mch proteins reside in intracellular membranes. However, pyruvate uptake into isolated mitochondria was not affected in the mchl-5 mutant strain. It is concluded that the yeast **monocarboxylate transporter**-homologous proteins perform other **functions** than do their mammalian counterparts. Copyright (C) 2001 John Wiley & Sons, Ltd.

L10 ANSWER 17 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2000:374572 SCISEARCH

THE GENUINE ARTICLE: 313LL

TITLE: An endogenous monocarboxylate transport in *Xenopus laevis* oocytes

AUTHOR: Tosco M (Reprint); Orsenigo M N; Gastaldi G; Faelli A

CORPORATE SOURCE: UNIV MILAN, DIPARTIMENTO FISIOL & BIOCHIM GEN, VIA CELORIA 26, I-20133 MILAN, ITALY (Reprint); UNIV PAVIA, IST FISIOL UMANA, I-27100 PAVIA, ITALY

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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We investigated the existence of an endogenous system for lactate transport in *Xenopus laevis* oocytes. Cl-36-uptake studies excluded the involvement of a DIDS-sensitive anion antiporter as a possible pathway for lactate movement. L-[C-14]lactate uptake was unaffected by superimposed pH gradients, stimulated by the presence of Na⁺ in the incubating solution, and severely reduced by the **monocarboxylate transporter** inhibitor p-chloromercuribenzenesulphonate (pCMBS). Transport exhibited a broad cation specificity and was cis inhibited by other monocarboxylates, mostly by pyruvate. These results suggest that lactate uptake is mediated mainly by a transporter and that the preferred anion is pyruvate. [C-14]pyruvate uptake exhibited the same pattern of **functional** properties evidenced for L-lactate. Kinetic parameters were calculated for both monocarboxylates, and a higher affinity for pyruvate was revealed. Various inhibitors of **monocarboxylate transporters**

reduced significantly pyruvate uptake. These studies demonstrate that *Xenopus laevis* oocytes possess a monocarboxylate transport system that shares some **functional** features with the members of the mammalian monocarboxylate cotransporters **family**, but, in the meanwhile, exhibits some particular properties, mainly concerning cation specificity.

L10 ANSWER 18 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
 ACCESSION NUMBER: 1999:529563 SCISEARCH
 THE GENUINE ARTICLE: 212HH
 TITLE: Lactate transport in skeletal muscle - role and regulation of the monocarboxylate transporter
 AUTHOR: Juel C; Halestrap A P (Reprint)
 CORPORATE SOURCE: UNIV BRISTOL, SCH MED SCI, DEPT BIOCHEM, BRISTOL BS8 1TD, AVON, ENGLAND (Reprint); UNIV BRISTOL, SCH MED SCI, DEPT BIOCHEM, BRISTOL BS8 1TD, AVON, ENGLAND; UNIV COPENHAGEN, AUGUST KROGH INST, COPENHAGEN MUSCLE RES CTR, DK-2100 COPENHAGEN, DENMARK
 COUNTRY OF AUTHOR: ENGLAND; DENMARK
 SOURCE: JOURNAL OF PHYSIOLOGY-LONDON, (15 JUN 1999) Vol. 517, No. 3, pp. 633-642.
 Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
 ISSN: 0022-3751.
 DOCUMENT TYPE: General Review; Journal
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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Skeletal muscle is the major producer of lactic acid in the body, but its oxidative fibres also use lactic acid as a respiratory fuel. The stereoselective transport of L-lactic acid across the plasma membrane of muscle fibres has been shown to involve a proton-linked **monocarboxylate transporter** (MCT) similar to that described in erythrocytes and other cells. This transporter plays an important role in the pH regulation of skeletal muscle. A **family** of eight MCTs has now been cloned and sequenced, and the tissue distribution of each isoform varies. Skeletal muscle contains both MCT1 (the only isoform found in erythrocytes but also present in most other cells) and MCT4. The latter is found in all fibre types, although least in more oxidative red muscles such as soleus, whereas expression of MCT1 is highest in the more oxidative muscles and very low in white muscles that are almost entirely glycolytic. The properties of MCT1 and MCT2 have been described in some detail and the latter shown to have a higher affinity for substrates. MCT4 has been less well characterized but has a lower affinity for L-lactate (i.e. a higher K_m, of 20 mM) than does MCT1 (K_m of 5 mM). MCT1 expression is increased in response to chronic stimulation and either endurance or explosive exercise training in rats and humans, whereas denervation decreases expression of both MCT1 and MCT4. The mechanism of regulation is not established, but does not appear to be accompanied by changes in mRNA concentrations. However, in other cells MCT1 and MCT4 are intimately associated with an ancillary protein OX-47 (also known as CD147). This protein is a member of the immunoglobulin **superfamily** with a single transmembrane helix, whose expression is known to be increased in a range of cells when their metabolic **activity** is increased.

L10 ANSWER 19 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
 ACCESSION NUMBER: 1998:695293 SCISEARCH
 THE GENUINE ARTICLE: 116VX
 TITLE: Monocarboxylate transporter expression in mouse brain

AUTHOR: KoehlerStec E M (Reprint); Simpson I A; Vannucci S J;
Landschulz K T; Landschulz W H

CORPORATE SOURCE: NIDDKD, EXPT DIABET METAB & NUTR SECT, DIABET BRANCH, NIH,
BLDG 10, RM 5N102, 10 CTR DR, MSC 1420, BETHESDA, MD 20892
(Reprint); PENN STATE UNIV, MILTON S HERSHEY MED CTR,
HERSHEY, PA 17033; UNIV TEXAS, SW MED CTR, DALLAS, TX
75235

COUNTRY OF AUTHOR: USA

SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND
METABOLISM, (SEP 1998) Vol. 38, No. 3, pp. E516-E524.
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REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although glucose is the major metabolic fuel needed for normal brain **function**, monocarboxylic acids, i.e., lactate, pyruvate, and ketone bodies, can also be utilized by the brain as alternative energy substrates. In most mammalian cells, these substrates are transported either into or out of the cell by a **family** of **monocarboxylate transporters** (MCTs), first cloned and sequenced in the hamster. We have recently cloned two MCT isoforms (MCT1 and MCT2) from a mouse kidney cDNA library. Northern blot analysis revealed that MCT1 mRNA is ubiquitous and can be detected in most tissues at a relatively constant level. MCT2 expression is more limited, with high levels of expression confined to testes, kidney, stomach, and liver and lower levels in lung, brain, and epididymal fat. Both MCT1 mRNA and MCT2 mRNA are detected in mouse brain using antisense riboprobes and in situ hybridization. MCT1 mRNA is found throughout the cortex, with higher levels of hybridization in hippocampus and cerebellum. MCT2 mRNA was detected in the same areas, but the pattern of expression was more specific. In addition, MCT1 mRNA, but not MCT2, is localized to the choroid plexus, ependyma, microvessels, and white matter structures such as the corpus callosum. These results suggest a differential expression of the two MCTs at the cellular level.

=> d his

(FILE 'HOME' ENTERED AT 14:04:47 ON 04 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:07:00 ON 04 MAR 2004

L1 997 S MONOCARBOXYLATE(W)TRANSPORTER?
L2 8 S SLC16
L3 5 DUP REM L2 (3 DUPLICATES REMOVED)
L4 113 S L1(S) (FAMILY OR SUPERFAMILY)
L5 40 DUP REM L4 (73 DUPLICATES REMOVED)
L6 214 S MCT4 OR MCT!4
L7 190 S L6 AND L1
L8 67 DUP REM L7 (123 DUPLICATES REMOVED)
L9 10 S L5 AND L8
L10 19 S L5 AND (FUNCTION? OR ACTIVIT?)

=>

---Logging off of STN---

10/074547

04/03/2004

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	77.22	78.06
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.08	-2.08

STN INTERNATIONAL LOGOFF AT 14:11:38 ON 04 MAR 2004